S.N. 10/069,400

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      (FILE 'HOME' ENTERED AT 09:57:42 ON 06 MAY 2003)

      FILE 'CAPLUS' ENTERED AT 09:57:54 ON 06 MAY 2003
                E HOFFMANN HANS/IN,AU
L1          113 S E3-4 OR E29-30
                E ASMUSSENBODO/IN,AU
                E ASMUSSEN BODO/IN,AU
L2           83 S E1-4
L3        14181 S CHITOSAN
L4          186 S L1 OR L2
L5            2 S L3 AND L4
L6           53 S NANOSOL OR (NANO SOL)
L7            1 S L4 AND L6
L8            2 S L6 AND L3
L9            1 S L8 NOT L5
L10       62823 S COLLOID
L11       95626 S COLLOIDAL
L12      137145 S L10 OR L11
L13         316 S L12 AND L3
L14      796635 S SOLUBLE OR SOLUBILIZ? OR SOLUBILITY
L15          68 S L14 AND L13
L16           1 S 2001:150590/AN
L17       86430 S DRUG DELIVERY

=> s l13 and l17
L18          36 L13 AND L17

=> d ibib ab 1-36

L18  ANSWER 1 OF 36  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2003:317455  CAPLUS
TITLE:                   Stabilization of liposomes mixtures and emulsions by
                         encapsulation of liposomes
INVENTOR(S):             Panzner, Steffen; Endert, Gerold; Lutz, Silke
PATENT ASSIGNEE(S):      Novosom AG, Germany
SOURCE:                  Eur. Pat. Appl., 7 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:           Patent
LANGUAGE:                German
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     EP 1304160         A1   20030423      EP 2002-90359    20021021
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.:                   DE 2001-10152145 A  20011019
AB   The invention concerns mixts. contg. two different types of
     colloidal particles; at least one type of the colloidal
     particles is nanocapsulated with a polymer layer. The polymer layer
     includes at least two water-sol. polymers. Polymer-encapsulated liposomes
     in O/W emulsions are prepd.; the encapsulation prevents the aggregation of
     the two different types of liposomes. Thus liposomes were prepd. from
     distearoyl phosphatidylglycerol and cholesterol (A) and distearoyl
     phosphatidylcholine and cholesterol (B). Liposomes A were encapsulated in
     chitosan-alginate layers in several cycles. The aggregation of
     the particles was measured; in case the nanoencapsuled liposome was in the
     mixt. with liposome B, no aggregation was measured as opposed to the mixt.
     of two non-encapsulated liposomes.
REFERENCE COUNT:         4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18  ANSWER 2 OF 36  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2003:238387  CAPLUS
DOCUMENT NUMBER:         138:292503
TITLE:                   Design of nano-particulate systems for drug
                         delivery
AUTHOR(S):               Takeuchi, Hirofumi
CORPORATE SOURCE:        Gifu Pharm. Univ., Gifu, 502-8585, Japan
SOURCE:                  Funtai Kogaku Kaishi (2003), 40(3), 185-191
                         CODEN: FKKADA; ISSN: 0386-6157
PUBLISHER:               Funtai Kogakkai
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                Japanese
AB   A review on design of nano-particulate liposomes for colloidal
     drug delivery system, discussing surface modification of
     liposomes, circulation profiles of polymer-coated liposomes, passive
     targeting of antitumor doxorubicin with polymer-coated liposomes,
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absorbability and enteric behavior of mucoadhesive liposomes coated with chitosan for orally administrated peptide drug delivery.

L18 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:173483 CAPLUS
DOCUMENT NUMBER: 138:226724
TITLE: Bioadhesive compositions for enhanced mucosal drug absorption
INVENTOR(S): Teng, Ching-leou; Weinbach, Susan P.; Tillman, Lloyd G.; Geary, Richard S.; Hardee, Gregory E.
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018134	A2	20030306	WO 2002-US26925	20020822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003083286	A1	20030501	US 2001-935316	20010822

PRIORITY APPLN. INFO.: US 2001-935316 A2 20010822

AB Compns. for enhanced mucosal drug absorption comprise a first population of carrier particles comprising a drug and a bioadhesive compd. and a second population of carrier particles comprising a penetration enhancer. The bioadhesive extends the residence time of the drug and its absorptive potential across the portion of, e.g., the intestinal mucosa made permeable by the penetration enhancer. For example, beads comprising an antisense oligonucleotide and bioadhesive agents (sticky beads) were formulated. Oligonucleotide (55% wt./wt.) was melted with polyethylene glycol 3500 (15% wt./wt.) to form granules. The granules were combined with the bioadhesives Carbopol 934 (15% wt./wt.) and Methocel E4M (15% wt./wt.) with or without the lubricants magnesium stearate and/or colloid silicon dioxide (Cab-O-Sil), then compressed into slugs. The slugs were broken into granules that were put through a sieve and particles having a size range of 200-600 .mu.m were collected to produce sticky beads. These beads are sticky due to the presence of the bioadhesive agents on their surface. The lubricants were added to prevent the granules from sticking together.

L18 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:146826 CAPLUS
DOCUMENT NUMBER: 138:158772
TITLE: Colon-releasing oral preparation and its preparing method
INVENTOR(S): Zhang, Junshou
PATENT ASSIGNEE(S): Zhang, Hao, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 19 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1326733	A	20011219	CN 2000-117989	20000607
WO 2002039982	A1	20020523	WO 2001-CN919	20010607
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

AU 2001072314 A5 20020527 AU 2001-72314 20010607
EP 1297828 A1 20030402 EP 2001-951330 20010607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: CN 2000-117989 A 20000607
WO 2001-CN919 W 20010607

AB The colon-releasing capsule or tablet is composed of medicine, metal salt (such as Ca, Fe, or Zn; its content of 5-12%) of pectin as coating, and medicinal carrier or excipient, poly(acrylic acid) coating, and/or general capsule shell (its water content of 6-10%). The process comprises mixing medicine with excipient or additive to obtain micro-pill, coating with metal salt of pectin, coating with poly(acrylic acid)/ethanol soln., and filling in gelatin capsule. The process may comprise mixing low-methoxy pectin with crosslinking agent (such formaldehyde, glutaraldehyde, Na alginate, gelatin, acacia, or **chitosan**, etc.) and plasticizing agent (such as propanediol, glycerol, di-Et phthalate, or castor oil, etc.) in water at 50.degree.C to obtain **colloid** soln., immersing liq. paraffin-coated mold bar in for 15 s-1 min, curing the mold bar in 0.1-10% ethanol metal salt soln. at 40-80.degree.C for 10 min-5 h, drying at 30-60.degree.C and RH 30-40% to water content of 6-10%, and/or immersing successively in 1-10% (w/v) polyvinylpyrrolidone soln. and 1-10% acrylic resin, drying to obtain capsule shell, and filling the medicine in.

L18 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:98245 CAPLUS
DOCUMENT NUMBER: 138:243069
TITLE: Labeling of Biocompatible Polymer Microcapsules with Near-Infrared Emitting Nanocrystals
AUTHOR(S): Gaponik, Nikolai; Radtchenko, Igor L.; Gerstenberger, Maria R.; Fedutik, Yuri A.; Sukhorukov, Gleb B.; Rogach, Andrey L.
CORPORATE SOURCE: Institute of Physical Chemistry, University of Hamburg, Hamburg, D-20146, Germany
SOURCE: Nano Letters (2003), 3(3), 369-372
CODEN: NALEFD; ISSN: 1530-6984
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Microcapsules consisting solely of biocompatible components were prepd. in water by a **colloidal** templating technique on sol. carbonate cores using alginic acid sodium salt, protamine sulfate, dextran sulfate, and **chitosan**. These microcapsules, as well as capsules made from synthetic polyelectrolytes, were labeled with water-sol. CdTe nanocrystals (NCs) emitting in the visible and, for the first time, with CdxHg1-xTe or HgTe NCs emitting in the near-IR. The luminescence efficiency of NCs at physiol. conditions remained stable for two weeks in the case of CdTe and at least for a month for CdHgTe and dropped by 80% for HgTe because of the shift of the luminescence band outside the water transmission window. Biocompatible microcapsules labeled with CdxHg1-xTe NCs emitting at 750-1200 nm might be of special interest for monitoring the **drug delivery** processes.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:22715 CAPLUS
DOCUMENT NUMBER: 138:61373
TITLE: Modified-release oral pharmaceutical compositions
INVENTOR(S): Massironi, Maria Gabriella
PATENT ASSIGNEE(S): Farmatron Ltd., UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002151	A1	20030109	WO 2002-EP6749	20020619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: IT 2001-MI1337 A 20010626
AB The present invention relates to modified-release oral pharmaceutical compns. contg. 1 or more active drugs solubilized, suspended or embedded in a suitably formulated amphiphilic matrix which, loaded in hydrophilic matrixes, provides different release profiles. Gelucire 44/14 (45 g) is melted and kept at 55-65.degree., 5 g Transcutol is added and the stirred mixt. is mixed with 5 g dioctyl sodium sulfosuccinate and 10 g .beta.-cyclodextrin. Calcium folinate (75 g) is loaded into a granulator/homogenizer and the hot mixt. obtained above is added thereto. The mixt. is granulated to homogeneity, then 100 g hydroxypropyl Me cellulose and 50 mg Polycarbophil are added in the granulator. The components are mixed to a homogeneous dispersion of the matrixes, then 210 g of Prosolv, 5 g magnesium stearate and 5 g **colloidal** silica are added in succession. The final mixt. is tabletted to a unitary wt. of 510 mg/tablet, so that 75 mg active ingredient/single tablet are administered.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:1669 CAPLUS
DOCUMENT NUMBER: 138:142370
TITLE: Layer-by-Layer Engineering of Biocompatible, Decomposable Core-Shell Structures
AUTHOR(S): Shenoy, Dinesh B.; Antipov, Alexei A.; Sukhorukov, Gleb B.; Mohwald, Helmuth
CORPORATE SOURCE: Max Planck Institute of Colloids and Interfaces, Potsdam/Golm, D-14424, Germany
SOURCE: Biomacromolecules (2003), 4(2), 265-272
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present investigation was to fabricate composite **colloidal** particles consisting of a sacrificial, decomposable template of biodegradable nature covered with biocompatible polyelectrolyte multilayers using the layer-by-layer sequential adsorption technique. Poly-DL-lactic acid and poly(DL-lactic-co-glycolic acid) were chosen to design the microparticulate template, and a preliminary feasibility study was carried out with poly(styrene sulfonate sodium)-poly(allylamine hydrochloride) as shell components. The properties of both core-shell and hollow structures obtained by core dissoln. were characterized by confocal laser scanning microscopy, microelectrophoresis, scanning force microscopy, and SEM. The concept was then extended to biocompatible polyelectrolytes as shell wall building blocks to deduce stable hollow capsules with tailored properties. Uniform, complete coating with oppositely charged polyelectrolyte pairs was achieved for all the combinations investigated. The results demonstrate that polyester microparticles could serve as viable alternative components to conventionally employed templates to derive hollow capsules with defined size, shape, and shell thickness. With all the components used for fabrication being biocompatible, these polyelectrolyte capsules may find interesting applications in the fields of biol., biochem., biotechnol., and **drug delivery**.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:904322 CAPLUS
DOCUMENT NUMBER: 137:389152
TITLE: Simethicone and polysorbate 80 as weight gain enhancers for coating compositions
INVENTOR(S): Szymczak, Christopher; Gulian, Cynthia; Gowan, Walter G., Jr.
PATENT ASSIGNEE(S): McNeil-PPC, Inc., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1260217	A2	20021127	EP 2002-253340	20020514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003070584	A1	20030417	US 2002-122999	20020412
US 2003072729	A1	20030417	US 2002-122498	20020415

PRIORITY APPLN. INFO.: US 2001-291127P P 20010515
US 2001-325726P P 20010928
US 2002-122999 A 20020412
US 2002-122498 A 20020415

AB A film forming compn. comprised of (i) a film former, selected from polyvinyl alc., starch derivs., pullulan, cellulose derivs., etc., and (b) a wt. gain enhancer, selected from simethicone, polysorbate 80 and their mixts., is described. The wt. gain enhancer is used in an amt. sufficient to increase the wt. gain of the film forming compn. on a substrate when dried. The film forming compn. further comprises a hydrocolloid, selected from alginates, natural gums, pectin, chitin, cyclodextrin, **chitosan**, etc., and a coloring agent, selected from azo, quinophthalone, triphenylmethane, xanthene or indigoid dyes, iron oxides, iron hydroxides, titanium dioxide, and natural dyes. For example, the film forming compn. contains 40-99.9% of a hydroxypropyl Me cellulose film former, 0.5-5% of a xanthan gum hydrocolloid, and 0.01-0.25% simethicone.

L18 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:629625 CAPLUS
DOCUMENT NUMBER: 138:276048
TITLE: Multilayer hollow microspheres
AUTHOR(S): Sukhorukov, Gleb B.
CORPORATE SOURCE: Max Planck Institute of Colloid and Interfaces, Potsdam, Germany
SOURCE: Microspheres, Microcapsules & Liposomes (2002), 5(Dendrimers, Assemblies, Nanocomposites), 111-147
CODEN: MMLIFU; ISSN: 1461-1732
PUBLISHER: Citus Books
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. This chapter presents a general review of solid and hollow nano- and microspheres (or nano- and microcapsules, MICs) obtained via layer by layer adsorption of oppositely charged polyelectrolytes (PELs) on template nano- and microparticles. Encapsulation of different templates from 50 nm to tens of microns, including org. and inorg. **colloidal** particles, protein aggregates, biol. cells and drug nanocrystals in synthetic PELs, **chitosan**, proteins, DNA and magnetic nanoparticles is discussed. The resulting MICs may be useful per se, or their core templates can be dissolved or decompd. to produce the corresponding hollow nanospheres or MICs with defined size, shape, shell thickness and permeability. PEL shells of these MICs have selective permeability, hence the possibility of again encapsulating various active agents for use in, among others, controlled and targeted delivery of active agents and microreactors for (bio)chem. reactions.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:615383 CAPLUS
DOCUMENT NUMBER: 137:145628
TITLE: Method for producing a floating tablet containing alfuzosin
INVENTOR(S): Bordes, Frederique; Cuart, Sylvie; Terrassin, Laurent
PATENT ASSIGNEE(S): Ellipse Pharmaceuticals, Fr.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062321	A2	20020815	WO 2002-FR474	20020207
WO 2002062321	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2820318	A1	20020809	FR 2001-1711	20010208
FR 2820319	A1	20020809	FR 2001-16705	20011221

PRIORITY APPLN. INFO.: FR 2001-1711 A 20010208
FR 2001-16705 A 20011221

AB The invention relates to a method for producing a tablet contg. alfuzosin,

which is characterized in that it comprises the following steps: a given quantity of alfuzosin is prepd. in accordance with the dosage for a given dissoln. time; said quantity of active principle is homogeneously mixed with a quantity of carrier of between 50 and 99.9% of the total wt., said carrier being chosen from among at least one compd. from the family of cellulose derivs. and/or povidone derivs. and/or polyvinyl acetate derivs.; said mixt. is compressed with a force in order to produce a homogeneous monolithic tablet that floats immediately in the gastric medium. The invention also covers the tablet obtained. Tablets contg. alfuzosin hydrochloride 10 mg, and hydroxypropyl Me cellulose 390 mg were compressed according to above method and their soln. rate was studied.

L18 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:441768 CAPLUS
DOCUMENT NUMBER: 138:193105
TITLE: Hydrogel-based **colloidal** polymeric system for protein and **drug delivery**: physical and chemical characterization, permeability control and applications
AUTHOR(S): Prokop, Ales; Kozlov, Evgenii; Carlesso, Gianluca; Davidson, Jeffrey M.
CORPORATE SOURCE: Chemical Engineering Department, Vanderbilt University, Nashville, TN, 37235, USA
SOURCE: Advances in Polymer Science (2002), 160(Filled Elastomers Drug Delivery Systems), 119-173
CODEN: APSIDK; ISSN: 0065-3195
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of polymeric nanoparticles as drug carriers is receiving an increasing amt. of attention both in academia and industry. The development of suitable delivery systems for protein drugs with high mol. wts. and short half-lives is of current interest. In addn., nanoparticles have a no. of potential applications in drug and vaccine delivery as well as gene therapy applications. This article features a new prodn. technol. for nanoparticles comprised of multicomponent polymeric complexes that are candidates for delivery vehicles of biol. mols. such as proteins and drugs. Materials science theory and practice provide the basis for the development of highly compacted structures that are insol. in water and buffered media. Biocompatible and mostly natural polymers are fabricated into thermodynamically stable nanoparticles, in the absence of org. solvents, using two types of processing: batch and continuous. Careful choice of construction materials and the superposition of several interacting principles during their prodn. allow for the customization of the physicochem. properties of the structures. Among the typical polymers used to assemble nanoparticles, different polysaccharides, natural amines and polyamines were investigated. The entrapped substances tested included proteins, antigens and small drug mols. The size and charge of nanoparticles is considered to be of primary importance for application in biol. systems. Detailed expts. in batch and continuous systems allowed time-dependent stoichiometric characterization of the prodn. process and an understanding of fundamental assembly principles of such supramol. structures. Continuous-flow prodn. is shown to provide more consistent data in terms of product quality and consistency, with further possibilities of process development and commercialization. To control permeability, polydextran aldehyde, incorporated into the particle core, was used to enable physiol. crosslinking and long-term retention of substances that would otherwise rapidly leak out of the nanoparticles. Results of crosslinking expts. clearly demonstrated that the release rate could be substantially reduced, depending on the degree of crosslinking. For vaccine antigen delivery tests we measured an antibody prodn. following s.c. and oral administration. The data indicated that only the cross-linked antigen was immunogenic when the oral route of administration was used. The data presented in this paper address primarily the utility of nanoparticulates for oral delivery of vaccine antigen. This novel technol. is extensively discussed in contrast to other technologies, primarily water- and org. solvent-based. The usefulness is demonstrated using several examples, evaluating protein and small **drug delivery**.
REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:122790 CAPLUS
DOCUMENT NUMBER: 136:189344
TITLE: Novel pharmaceutical compositions of antitubercular drugs and process for their preparation
INVENTOR(S): Singh, Amarjit; Jain, Rajesh
PATENT ASSIGNEE(S): Panacea Biotec Limited, India

SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011728	A2	20020214	WO 2001-IN89	20010410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001056661	A5	20020218	AU 2001-56661	20010410
BR 2001007147	A	20020618	BR 2001-7147	20010410
NO 2002001599	A	20020610	NO 2002-1599	20020404
US 2003072800	A1	20030417	US 2002-110134	20020409
BG 106606	A	20021229	BG 2002-106606	20020411

PRIORITY APPLN. INFO.: IN 2000-DE720 A 20000809
WO 2001-IN89 W 20010410

AB An oral pharmaceutical compn. of antitubercular drugs with enhanced bioavailability comprises Rifampicin and/or isoniazid. Preferably the bioavailability of Rifampicin is enhanced by preventing its degrdn. caused by presence of isoniazid. Rifampicin and/or isoniazid may be present in delayed release and/or extended release form such that minimal amt. of the drug is dissolved at pH 1-4; preferably delayed release of Rifampicin and/or isoniazid is achieved by treating the drugs with pH-sensitive polymers. For example, a bilayer tablet contg. isoniazid in extended release form was prepd. by granulating isoniazid 0.150 g, hydroxypropyl Me cellulose 0.050 g, and iso-Pr alc. 2.000 g (Layer I), and Rifampicin 0.225 g, ethambutol-HCl 0.400 g, pyrazinamide 0.750 g, starch 0.075 g, and water 0.500 g (Layer II). Granulates were dried and compressed into bilayered tablets. Rifampicin (Layer II) was immediately released while isoniazid layer was released in delayed form. Also, an antitubercular formulation in kit form contained (A) one enteric-coated tablet of Rifampicin 150 mg, and (B) one film-coated tablet contg. isoniazid 150 mg, ethambutol-HCl 400 mg, and pyrazinamide 750 mg, or (A) one enteric-coated tablet of isoniazid 150 mg, and (B) one film-coated tablet contg. Rifampicin 225 mg, ethambutol-HCl 400 mg, and pyrazinamide 750 mg.

L18 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:57382 CAPLUS
DOCUMENT NUMBER: 137:37522
TITLE: **Colloid**-chemical aspects of the production of microcapsules and gel beads from insoluble surfactant-**chitosan** complexes
AUTHOR(S): Babak, Valery G.; Merkovich, Elena A.
CORPORATE SOURCE: INEOS RAS, Moscow, Russia
SOURCE: World Surfactants Congress, 5th, Firenze, Italy, May 29-June 2, 2000 (2000), 676-682. Comite Europeen des Agents de Surface et leurs Intermediaires Organiques: Brussels, Belg.
CODEN: 69BYUW
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English

AB Prodn. of pH- and thermo-sensitive carriers (nano- and microcapsules) on the base of phys. hydrogels made from insol. complexes between anionic or cationic polysaccharides and oppositely charged surfactants (e.g. fatty acids, phospholipids, etc.) may be interesting for medicine, cosmetics, food industry. These vectors may be loaded by bioactive principles (enzymes, living cells, etc.) in their aq. core, and contain in their gel-like walls the micelle-like aggregates able to be solubilized by the oil-sol. drugs. The objective of this work was to give more insight to the kinetics of the formation and to the structure-mech. properties of microcapsules walls made from insol. surfactant-polysaccharide complexes on the base of **chitosan**.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:522479 CAPLUS
DOCUMENT NUMBER: 135:298174
TITLE: **Chitosan** as a nonviral gene delivery system. Structure-property relationships and characteristics

compared with polyethylenimine in vitro and after lung administration in vivo

AUTHOR(S): Koping-Hoggard, M.; Tubulekas, I.; Guan, H.; Edwards, K.; Nilsson, M.; Varum, K. M.; Artursson, P.

CORPORATE SOURCE: Department of Pharmacy, Division of Pharmacy, Uppsala University, Uppsala, Swed.

SOURCE: Gene Therapy (2001), 8(14), 1108-1121
CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Chitosan** is a natural cationic linear polymer that has recently emerged as an alternative nonviral gene delivery system. We have established the relationships between the structure and the properties of **chitosan**-pDNA polyplexes in vitro. Further, we have compared polyplexes of ultrapure **chitosan** (UPC) of preferred mol. structure with those of optimized polyethylenimine (PEI) polyplexes in vitro and after intratracheal administration to mice in vivo. **Chitosans** in which over two out of three monomer units carried a primary amino group formed stable **colloidal** polyplexes with pDNA. Optimized UPC and PEI polyplexes protected the pDNA from serum degrdn. to approx. the same degree, and they gave a comparable maximal transgene expression in 293 cells. In contrast to PEI, UPC was non toxic at escalating doses. After intratracheal administration, both polyplexes distributed to the mid-airways, where transgene expression was obsd. in virtually every epithelial cell, using a sensitive pLacZ reporter contg. a translational enhancer element. However, the kinetics of gene expression differed - PEI polyplexes induced a more rapid onset of gene expression than UPC. This was attributed to a more rapid endosomal escape of the PEI polyplexes. Although this resulted in a more efficient gene expression with PEI polyplexes, UPC had an efficiency comparable to that of commonly used cationic lipids. In conclusion, this study provides insights into the use of **chitosan** as a gene delivery system. It emphasizes that **chitosan** is a nontoxic alternative to other cationic polymers and it forms a platform for further studies of **chitosan** -based gene delivery systems.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:254826 CAPLUS

DOCUMENT NUMBER: 134:271275

TITLE: Membrane-forming **colloids** for the treatment of wound

INVENTOR(S): Kawanishi, Takashi; Takao, Kota; Tsuji, Yuji; Shirokane, Hideki

PATENT ASSIGNEE(S): Kobayashi Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001097848	A2	20010410	JP 1999-280707	19990930

PRIORITY APPLN. INFO.: JP 1999-280707 19990930

AB This invention relates to topical compns. in the form of hydrophilic **colloids** contg. water-sol. polymers and liquefied hydrocarbons. The compns. are sprayed on an affected area and quickly form the dry coat, which can be easily washed out with water. An aerosol was formulated contg. gelatin 10, tara gum 5, squalane 20, isopropylmethylphenol 4, chitin 1, fructose 20, and liquefied butane gas 40 %.

L18 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:2221 CAPLUS

DOCUMENT NUMBER: 134:242535

TITLE: Niosomes and polymeric **chitosan** based vesicles bearing transferrin and glucose ligands for drug targeting

AUTHOR(S): Dufes, Christine; Schatzlein, Andreas G.; Tetley, Laurence; Gray, Alexander I.; Watson, Dave G.; Olivier, Jean-Christophe; Couet, William; Uchegbu, Ijeoma F.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, Glasgow, G4 0NR, UK

SOURCE: Pharmaceutical Research (2000), 17(10), 1250-1258
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polymeric vesicles and niosomes bearing glucose or transferrin ligands were prepd. for drug targeting. A glucose-palmitoyl glycol **chitosan** (PGC) conjugate was synthesized and glucose-PGC polymeric vesicles prepd. by sonication of glucose-PGC/ cholesterol. N-palmitoylglucosamine (NPG) was synthesized and NPG niosomes also prepd. by sonication of NPG/ sorbitan monostearate/ cholesterol/ cholesteryl poly-24-oxyethylene ether. These 2 glucose vesicles were incubated with **colloidal** Con A gold (Con-A gold), washed and visualized by transmission electron microscopy (TEM). Transferrin was also conjugated to the surface of PGC vesicles and the uptake of these vesicles investigated in the A431 cell line (over expressing the transferrin receptor) by fluorescent activated cell sorter anal. TEM imaging confirmed the presence of glucose units on the surface of PGC polymeric vesicles and NPG niosomes. Transferrin was coupled to PGC vesicles at a level of 0.60 .+-. 0.18 g of transferrin per g polymer. The proportion of FITC-dextran pos. A431 cells was 42% (FITC-dextran soln.), 74% (plain vesicles) and 90% (transferrin vesicles). Glucose and transferrin bearing **chitosan** based vesicles and glucose niosomes have been prepd. Glucose bearing vesicles bind Con-A to their surface. **Chitosan** based vesicles are taken up by A431 cells and transferrin enhances this uptake.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:573636 CAPLUS
DOCUMENT NUMBER: 133:182757
TITLE: Use of nanoscale **chitosans** and/or **chitosan** derivatives
INVENTOR(S): Kropf, Christian; Fabry, Bernd; Foerster, Thomas; Wachter, Rolf; Reil, Stephan; Panzer, Claudia
PATENT ASSIGNEE(S): Cognis Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047177	A1	20000817	WO 2000-EP720	20000129
W: AU, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1150655	A1	20011107	EP 2000-904985	20000129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002536392	T2	20021029	JP 2000-598130	20000129

PRIORITY APPLN. INFO.: US 1999-119512P P 19990209
WO 2000-EP720 W 20000129

AB **Chitosans** and/or **chitosan** derivs. with particle diams. of 10-300 nm are useful in cosmetic and/or pharmaceutical formulations as moisturizers and film-forming agents. The particularly small size of the particles ensures that when applied topically, they rapidly penetrate into the stratum corneum of the skin or the keratin fibrils of the hair. Thus, **chitosan** nanoparticles 50-125 nm in diam. were prepd. by rapid expansion of a supercrit. CO2 soln. of **chitosan** at 200 bar and 175.degree. into a 4 wt.% aq. soln. of poly(vinyl alc.). A sunscreen cream was prepd. contg. Dehymuls PGPH 2.0, Lameform TGI 4.0, beeswax 3.0, Plantaren 818 5.0, dioctyl carbonate 5.0, Cetiol J 600 2.0, Cetiol OE 30, panthenol/bisabolol 1.2, **chitosan** nanoparticles 0.5, Neo Heliopan Hydro 3.0, Neo Heliopan BB 1.5, Neo Heliopan E 1000 5.0, Neo Heliopan AV 4.0, Uvinul T 150 2.0, 86% glycerin 5.0, preservative, and H2O to 100 wt.%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:190981 CAPLUS
DOCUMENT NUMBER: 132:224361
TITLE: Method for producing nanoparticles by expansion of supercritical solutions
INVENTOR(S): Kropf, Christian; Dolhaine, Hans; Forster, Thomas; Schaber, Karlheinz; Turk, Michael; Cihlar, Stephan; Christophliemk, Peter
PATENT ASSIGNEE(S): Henkel K.-G.a.A., Germany

SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015329	A1	20000323	WO 1999-EP6527	19990904
W: AU, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9957455	A1	20000403	AU 1999-57455	19990904

PRIORITY APPLN. INFO.: US 1998-100466P P 19980915
WO 1999-EP6527 W 19990904

AB Nanoparticles with 10-300 nm diam. are produced by dissolving org. active agents in a solvent in supercrit. or near-crit. conditions (400-100.degree.C, 20-200 bar); expanding the fluid mixt. into a gas or a liq. using a nozzle; and evapg. the solvent at the same time. Emulsifiers and/or protective **colloids** are used in prodn. and collection of the particles. The nanoparticles can be used in cosmetics and **drug delivery** systems.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:157862 CAPLUS
DOCUMENT NUMBER: 132:199065
TITLE: Pharmaceutical preparation containing **colloidal** polymer-active substance complexes, in particular for mucosal administration
INVENTOR(S): Kissel, Thomas; Breitenbach, Armin; Jung, Tobias; Kamm, Walter
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19839515	A1	20000309	DE 1998-19839515	19980829

PRIORITY APPLN. INFO.: DE 1998-19839515 19980829

AB Water-sol., biodegradable polyol esters form **colloidal** complexes with pharmacol. active proteins, glycoproteins, peptides, growth factors, oligonucleotides, and DNA constructs and are useful as carriers for these substances in pharmaceutical dosage forms. Lipophilic polyol esters are converted into nanoparticles by controlled pptn. and subsequently loaded with active substances for the same purpose. In both cases, the resulting active substance-contg. **colloids** show improved bioavailability, biodistribution, and effectiveness in human or veterinary applications after mucosal application. These carriers may also be useful for parenteral administration and transport of active substances to targeted sites in the body. Thus, a 1:1 M mixt. of DL-lactide and glycolide was melt-grafted onto poly(vinyl alc.) with various degrees of substitution. The resulting water-sol. ester formed a complex with tetanus toxoid, the particle size of which depended on ionic strength, pH, and the presence of emulsifiers.

L18 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:722274 CAPLUS
DOCUMENT NUMBER: 132:284036
TITLE: Study of the interaction and transport of various **colloidal** drug carriers through the cornea
AUTHOR(S): De Campos, A. Machado; Calvo, P.; Gref, R.; Alonso, M. J.
CORPORATE SOURCE: Dept. of Pharmaceutical Technology, Santiago de Compostela, 15706, Spain
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 351-352
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Poly(.epsilon.-caprolactone) nanocapsules cross the corneal epithelium by a transcellular mechanism. **Chitosan** coating increased the

corneal penetration of the encapsulated Rhodamine 6G.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:549162 CAPLUS
DOCUMENT NUMBER: 131:149343
TITLE: Process for preparing solid preparation by using **colloid** of platinum and palladium as main raw material and use thereof
INVENTOR(S): Kazama, Hiroshi; Yamazaki, Ichiro
PATENT ASSIGNEE(S): Ohtuka Chemical Industrial Co., Ltd., Japan
SOURCE: PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942112	A1	19990826	WO 1998-JP2621	19980615
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 11240839	A2	19990907	JP 1998-80098	19980223

PRIORITY APPLN. INFO.: JP 1998-80098 19980223
AB The invention relates to a **colloid** prepn. of platinum and palladium scavenges active oxygen and thus produces surprising effects for treatment and prevention of diseases, enhancement in vitality of the human body and improvement in health. Since, however, air and oxygen should be cut off for its stable storage, the prepn. should have been in the form of an ampoule. In the present invention, the internal surface of a capsule is coated with **chitosan** for protecting the **colloid** soln. of platinum and palladium against air and oxygen, i.e., cutting off air and oxygen. Specifically, an about 2% acidic soln. of **chitosan** having a mol. wt. of 500 to 5000 and dissolved under such an acidic condition that the pH is not more than 4 is sprayed on the internal surface of a gelatin film for the prepn. of a soft capsule, followed by drying to a small extent. For realizing the acidic condition, the use of an org. acid acceptable as a food additive is preferred. In the prepn. of a soft capsule, the use of a coating with the internal surface thereof being coated with **chitosan** can provide a soft capsule which enables an aq. soln., such as a **colloidal** soln. of platinum and palladium, to be encapsulated therein and can realize protection against air.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:525340 CAPLUS
DOCUMENT NUMBER: 131:314156
TITLE: Membrane Filtration for Microencapsulation and Microcapsules Fabrication by Layer-by-Layer Polyelectrolyte Adsorption
AUTHOR(S): Voigt, Andreas; Lichtenfeld, Heinz; Sukhorukov, Gleb B.; Zastrow, Heidemarie; Donath, Edwin; Baeumler, Hans; Moehwald, Helmuth
CORPORATE SOURCE: Max-Planck-Institute of Colloids and Interfaces, Potsdam, D-14424, Germany
SOURCE: Industrial & Engineering Chemistry Research (1999), 38(10), 4037-4043
CODEN: IECRED; ISSN: 0888-5885
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Layer-by-layer polyelectrolyte adsorption at **colloid** particle surfaces as well as the removal of the core latex to obtain multilayer microcapsules is conducted by means of membrane filtration. As target particles for adsorption we use nonsol. polystyrene sulfate latex, sol. melamine formaldehyde resin latex, and decomposable glutaraldehyde-fixed human red blood cells. The materials adsorbed are poly(allylamine hydrochloride), poly(styrenesulfonate), poly(diallyldimethylammonium chloride), **chitosan**, and chitosansulfate. The coating process is carried out under different membrane filtration conditions with respect to the pressure regime, the filter materials, and the stirring conditions. We characterize the prepd. multilayers at the particle surface or in the microcapsule (shell) form by at. force microscopy, confocal laser scanning microscopy, transmission electron microscopy, single-particle light scattering, and electrophoresis. The quality, performance, and yield of the presented method are compared with the results obtained by

centrifugation and sequential adsorption as alternative prepn. strategies. Membrane filtration surpasses all other methods, so far established, with respect to the above criteria.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:404822 CAPLUS
DOCUMENT NUMBER: 131:49485
TITLE: Preparation with a prolonged retention time at the site of application
INVENTOR(S): Bodmeier, Roland; Maincent, Philippe
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930683	A1	19990624	WO 1998-DE3739	19981211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19756314	A1	19990624	DE 1997-19756314	19971212
DE 19756314	C2	20000629		
AU 9924101	A1	19990705	AU 1999-24101	19981211
EP 1037606	A1	20000927	EP 1998-966561	19981211
R: AT, BE, CH, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1997-19756314 A 19971212
WO 1998-DE3739 W 19981211

AB Solid, rapidly disintegrating prepns. are provided which prolong the retention time at the site of application, e.g., a mucous membrane or the eye. The prepns. comprise an active agent enclosed within microparticles with a polymeric matrix; they may be extruded or compressed into pellets. On contact with body fluids, such a prepn. forms a viscous and/or bioadhesive mass which retains the active agent at the site of application. Thus, betaxolol was bound to ion exchanger (Amberlite IRP-69) particles which were then dispersed in a 5-10 wt.% gelatin soln. The dispersion was dispensed into blister packs, frozen, and lyophilized to produce a porous matrix which dispersed rapidly on addn. of water.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:311106 CAPLUS
DOCUMENT NUMBER: 130:357163
TITLE: Water-soluble polymer-based solid dispersions for lipid lowering agents
INVENTOR(S): Baert, Lieven; Verreck, Geert
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922738	A1	19990514	WO 1998-EP6998	19981027
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2307097	AA	19990514	CA 1998-2307097	19981027
AU 9911576	A1	19990524	AU 1999-11576	19981027
AU 746890	B2	20020502		
EP 1028730	A1	20000823	EP 1998-954483	19981027

EP 1028730 B1 20020417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
BR 9814109 A 20001003 BR 1998-14109 19981027
EE 200000186 A 20010416 EE 2000-20000018619981027
JP 2001521899 T2 20011113 JP 2000-518671 19981027
AT 216238 E 20020515 AT 1998-954483 19981027
ZA 9809997 A 20000502 ZA 1998-9997 19981102
BG 104338 A 20001229 BG 2000-104338 20000414
US 6342245 B1 20020129 US 2000-530170 20000424
NO 2000002279 A 20000428 NO 2000-2279 20000428
PRIORITY APPLN. INFO.: EP 1997-203407 A 19971103
WO 1998-EP6998 W 19981027

AB Pharmaceutical compns. for administration of lipid lowering agents once daily independently of the food intake for treatment of hyperlipidemia, obesity or atherosclerosis are described. These compns. comprise particles obtained by melt-extruding a mixt. comprising a lipid lowering agent and an appropriate water-sol. polymer and subsequent milling. E.g., a film-coated tablet formulation contained: (1) hypolipemic agent 100, HPMC 300, lactose/microcryst. cellulose (75:25) mixt. 226, crospovidone 62.8, talc 20.6, hydrogenated vegetable oil 6.8, **colloidal** silica 2, and Mg stearate 1.8 mg, resp., yielding a tablet core, and (2) HPMC 13.7, propylene glycol 3.4, talc 2.76, and TiO2 4.14 mg, resp., as a film coat.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:282688 CAPLUS
DOCUMENT NUMBER: 130:287051
TITLE: Wound protective film compositions and prepared thereof
INVENTOR(S): Wu, Xiangjin
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1114589	A	19960110	CN 1994-110380	19940707

PRIORITY APPLN. INFO.: CN 1994-110380 19940707

AB The title film compns. are composed of alginic acid, **chitosan**, dil. acid, base, and distd. water. The prepn. of the title film comprises mixing distd. water with alginic acid and adjusting to pH 7-8 with dil. base (NaOH) to give a clear **colloidal** soln., and mixing distd. water with **chitosan** and adjusting to pH 4.5 with dil. acid (trichloroacetic acid) to give another milky **colloidal** soln. The compns. contain: [a] alginic acid and distd. water at ratio 4-5:1000 and [b] **chitosan** and distd. water at ratio 9-10:1000. Wound treatment involves application of [a] and then [b] to form a film on the skin.

L18 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:48756 CAPLUS
DOCUMENT NUMBER: 130:129976
TITLE: Conjugate of polyethylene glycol and **chitosan**
INVENTOR(S): Davis, Stanley Stewart; Lin, Wu; Bignotti, Fabio; Ferruti, Paolo
PATENT ASSIGNEE(S): Danbiosyst UK Limited, UK
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901498	A1	19990114	WO 1998-GB1971	19980703

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, ML, MR, NE, SN, TD, TG

ZA 9805831	A	20000110	ZA 1998-5831	19980702
AU 9882305	A1	19990125	AU 1998-82305	19980703
EP 993483	A1	20000419	EP 1998-932368	19980703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508020	T2	20020312	JP 1999-506685	19980703
EP 1304346	A2	20030423	EP 2002-79756	19980703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: GB 1997-13980 A 19970703
EP 1998-932368 A3 19980703
WO 1998-GB1971 W 19980703

AB PEG-**chitosan** conjugates, which are pos. charged, can be used for delivery of anionic macromol. drugs such as antisense oligonucleotides and DNA, and for **colloidal drug delivery** through interaction with neg. charged surfaces and neg. charged **colloidal** surfaces. They can also provide increased absorption of drugs across mucosal surfaces through interaction with neg. charged mucus or neg. charged epithelial cell surfaces, and can be used for improved compaction of plasmid DNA into small particles for improved administration to cells. Thus, monomethoxy-PEG was converted with piperazine and 1,1'-carbonyldiimidazole to monomethoxy-PEG piperazinyl formate, then with acryloyl chloride to monomethoxy-PEG acrylamide, and finally with **chitosan**-HCl and 4-methoxyphenol to PEG-**chitosan**. PEG-**chitosan** was adsorbed to sulfated polystyrene nanoparticles (diam. 190 nm), as shown by a reversal in .zeta. potential of the particles; the coated particles were more resistant to flocculation with Na2SO4 than particles coated with **chitosan**.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:804165 CAPLUS
DOCUMENT NUMBER: 130:57200
TITLE: Multiphase system for controlled drug release
INVENTOR(S): Bodmeier, Roland
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855100	A1	19981210	WO 1998-DE1589	19980605
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19724784	A1	19981210	DE 1997-19724784	19970605
DE 19811951	A1	19990916	DE 1998-19811951	19980313
AU 9885304	A1	19981221	AU 1998-85304	19980605
EP 996426	A1	20000503	EP 1998-936136	19980605
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1997-19724784 19970605
DE 1998-19811951 19980313
WO 1998-DE1589 19980605

AB A multiphase system for formation of a drug-contg. implant in vivo comprises a carrier phase and .gtoreq.1 further phase which cannot be mixed with the carrier phase or only partially mixed therewith, wherein the change in ambient conditions on injection of the system alters (generally increases) the viscosity of the carrier phase, resulting in formation of an implant or particles enriched in carrier (and active agent). The change in ambient conditions may involve a change in pH, ionic species, ionic strength, temp., etc. The carrier is a water-sol. or -insol., biodegradable polymer, e.g. a polylactide, polysaccharide, protein, or lipid or combination thereof, and is dissolved or dispersed in the carrier phase. Thus, poly(DL-lactide) was dissolved in a mixt. of DMSO, PEG-400, and Tween 80 to form a carrier phase. A 2nd phase was prepd. by mixing 2% Al stearate with peanut oil at elevated temp., cooling, and adding Span 80. The 2 phases were combined to form an emulsion.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:738910 CAPLUS
DOCUMENT NUMBER: 130:172906
TITLE: Preparation of casein-**chitosan** microspheres containing diltiazem hydrochloride by an aqueous coacervation technique
AUTHOR(S): Bayomi, M. A.; Al-Suwayeh, S. A.; El-Helw, A. M.; Mesnad, A. F.
CORPORATE SOURCE: College of Pharmacy, Department of Pharmaceutics, King Saud University, Riyadh, 11451, Saudi Arabia
SOURCE: Pharmaceutica Acta Helvetiae (1998), 73(4), 187-192
CODEN: PAHEAA; ISSN: 0031-6865
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sustained release casein-**chitosan** microspheres contg. diltiazem-HCl (DTZ) were prepd. with **colloidal** coacervation technique in a completely aq. environment. The interaction between **chitosan** soln. in dil. HOAc (5%) and casein soln. in 0.5M sodium hydroxide was the basis for the microspheres formation. Formaldehyde was used for the surface hardening of the droplets by crosslinking and thus fixing the shape and surface morphol. of the formed microspheres. The entrapment efficiencies of the microspheres were variables (14.5-53.7%) depending on the prepn. conditions. The prepd. microspheres exhibited an angle of repose values between 31.9-42.0.degree. indicating good free flowing nature, whereas DTZ powder as such was non-flowable. The dissoln. profiles of DTZ from casein-**chitosan** microspheres showed retarded release pattern of the drug into distd. water. Casein and **chitosan** concns., initial drug concn. and stirring time were found to be the main parameters that affect the properties and the performance of the prepd. microspheres. The retarded release of DTZ was increased by increasing casein concn., and stirring time. On the other hand, increasing **chitosan** concn. and using high initial drug loading showed a fast drug release.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:706012 CAPLUS
DOCUMENT NUMBER: 129:321197
TITLE: Antiretroviral compositions comprising loviride with improved bioavailability
INVENTOR(S): Baert, Lieven Elvire Colette; Verreck, Geert
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 872233	A1	19981021	EP 1997-201100	19970414

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: EP 1997-201100 19970414
AB Novel pharmaceutical compns. of loviride (I) which can be administered to a patient suffering from a retroviral infection, whereby such dosage forms have a high drug content and can be administered at any time of the day independently of the food taken in by said patient are disclosed. These novel compns. comprise particles obtainable by melt-extruding a mixt. comprising loviride and an appropriate water-sol. polymer and subsequently milling said melt-extruded mixt. A melt-extruded mixt. comprising a 40:60 mixt. of (.+-.)-I:HPMC was prepd. The above melt-extruded 250 g was mixed with microcryst. cellulose 90.2, crospovidone 25, Aerosil 1.1, and Sterotex 3.7 g and were used to prep. tablet of 370 mg. The Cmax of (-)-I and (+)-I was 155, and 890 ng/mL, resp.; and the AUClast of (-)-I and (+)-I was 1347, and 18180 ng.h/mL, resp.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:625415 CAPLUS
DOCUMENT NUMBER: 129:335632
TITLE: Development of diclofenac sodium controlled release solid dispersion powders and capsules by freeze drying technique using ethyl cellulose and **chitosan** as carriers

AUTHOR(S): Dangprasirt, P.; Pongwai, S.
CORPORATE SOURCE: Faculty of Pharmacy, Rangsit Univ. Patumtani, 12000, Thailand
SOURCE: Drug Development and Industrial Pharmacy (1998), 24(10), 947-953
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Controlled-release, solid dispersions of diclofenac sodium (DS) were prepd. by freeze-drying technique, using Et cellulose (EC) and **chitosan** (CS) as single and combined carriers. Factorial design was applied as an exptl. design to study the main and interactive effects of EC and CS on drug dissoln. from the controlled release solid dispersion. All DS solid dispersions showed slower drug dissoln. than did DS powder. The equations of dissoln. parameters as functions of EC and CS contents were established through multiple regression. The contour plots of the established equations were constructed. The 10:(2.4 + 0.05) DS:(EC + CS) solid dispersion was prepd. and developed into a capsule dosage from, using lactose as diluent. The effect on capsule dissoln. of a disintegrant, sodium starch glycolate (Explotab), in concns. of 2%, 5%, and 8% was studied. The solid-dispersion capsule contg. 5% Explotab was found to provide the most similar dissoln. profile to the one obtained with the 10:(2.4 + 0.05) DS:(EC + CS) solid-dispersion powder. The dissolns. of the 10:(2.4 + 0.05) solid-dispersion powder and capsules were closer to a first-order model than to a zero-order or diffusion control model.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:360514 CAPLUS
DOCUMENT NUMBER: 129:126942
TITLE: The use of alginic acid and its salts in the pharmaceutical field
AUTHOR(S): Takka, Sevgi; Acarturk, Fusun
CORPORATE SOURCE: Eczacilik Fakultesi, Farmasotik Teknoloji Anabilim Dali, Gazi Universitesi, Ankara, Turk.
SOURCE: FABAD Farmasotik Bilimler Dergisi (1998), 23(1), 17-27
CODEN: FBDEDQ; ISSN: 1300-4182
PUBLISHER: Farmasotik Bilimler Ankara Dernegi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Turkish

AB A review with 91 refs. Alginic acid and its salts, alginates, are naturally hydrophilic **colloidal** polymers which were extd. from brown seaweed by Stanford in 1880. Alginates can be considered as block polymers. The different parts are referred to as M blocks, G blocks and MG blocks. One of te most useful properties of alginates is the ability to form gels. Addn. of di or polyvalent cations (except Mg++) to alginate sodium causes gel formation by crosslinking. Calcium, barium or strontium can be used as crosslinking agents. Alginates have been widely used in the food industry, textile processing, paper making, medicine, pharmaceutical technol. applications and also most commonly used at dental impression material. Alginates have received much attention in pharmaceutical prepns., particularly as a vehicle for controlled **drug delivery** of gel beads. The effect of the various formulation factors on the properties of gel beads and the release rate of drug from alginate-gel beads have been investigated by several authors. Some additive polymers such as **chitosan**, polylysine and polyacrylic acid can be used to control the release of drug from the beads. Alginates are also used as a matrix material for the encapsulation of microbial cells, enzymes and islets of Langerhans.

L18 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:163454 CAPLUS
DOCUMENT NUMBER: 128:221641
TITLE: Pharmaceutical controlled-release tablet containing alfuzosin hydrochloride
INVENTOR(S): Maggi, Lauretta; Conte, Ubaldo; Grenier, Pascal; Vergnault, Guy; Dufour, Alain; Jarreau, Francois Xavier; Rauch-Desanti, Clemence
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.; Jagotec A.-G.; Maggi, Lauretta; Conte, Ubaldo; Grenier, Pascal; Vergnault, Guy; Dufour, Alain; Jarreau, Francois Xavier; Rauch-Desanti, Clemence
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808515	A1	19980305	WO 1997-FR1515	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2752737	A1	19980306	FR 1996-10551	19960829
FR 2752737	B1	19981002		
AU 9740201	A1	19980319	AU 1997-40201	19970822
EP 938318	A1	19990901	EP 1997-937651	19970822
EP 938318	B1	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
CN 1228700	A	19990915	CN 1997-197558	19970822
BR 9713237	A	20000404	BR 1997-13237	19970822
JP 2000514462	T2	20001031	JP 1998-511331	19970822
IL 128146	A1	20010111	IL 1997-128146	19970822
AT 200864	E	20010515	AT 1997-937651	19970822
ES 2159400	T3	20011001	ES 1997-937651	19970822
RU 2183459	C2	20020620	RU 1999-105730	19970822
EE 3855	B1	20021015	EE 1999-90	19970822
ZA 9707766	A	19980223	ZA 1997-7766	19970828
NO 9900944	A	19990427	NO 1999-944	19990226
US 6149940	A	20001121	US 1999-147581	19990426
HK 1020875	A1	20011123	HK 1999-105968	19991220

PRIORITY APPLN. INFO.: FR 1996-10551 A 19960829
FR 1997-4386 A 19970410
WO 1997-FR1515 W 19970822

AB A pharmaceutical tablet for oral administration, for the controlled release of alfuzosin hydrochloride (I) at the proximal segments of the gastrointestinal tract, characterized in that it consists of: (a) a first layer capable of swelling noticeably and rapidly in contact with aq. biol. liqs., said layer being produced by a mixt. or a granule contg. hydrophilic polymers constituting 5.0 to 90 % and preferably 10 to 85 % of the layer wt.; (b) a second layer adjacent to or superposed on the first layer, in which is carried the I, this layer being formed with hydrophilic polymers and other auxiliary substances, so as to give to the prepn. suitable compressibility properties and to enable the release of the I in a predetd. lapse of time; (c) and optionally a third layer obtained by compression and applied on layer, generally consisting in particular of hydrophilic polymers which gel and/or swell and then can be optionally eroded and acting as a barrier modulating the release of the alfuzosin of second layer, the third layer being almost impermeable to the passage of the active substance. A controlled-release tablet contained I 10.00, mannitol 10.00, hydroxypropyl Me cellulose (II) 10.00, PVP 3.20, microcryst. cellulose 65.00, magnesium stearate 1.00, **colloidal** silica 1.25 mg in the second layer; II 79.75, hydrogenated castor oil (III) 13.50, yellow iron oxide (IV) 0.25, Et cellulose 5.00, magnesium stearate (V) 1.00, and silica gel 0.50% in the first layer; and II 76.00, III 18.60, PVP 3.15, IV 0.10, V 0.10, and **colloidal** silica 1.45% in the third layer. The amt. of I released after 24 h was 98%.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:708602 CAPLUS
DOCUMENT NUMBER: 127:351223
TITLE: Pharmaceutical preparation containing diphosphonic acids for oral application
INVENTOR(S): Moeckel, Joern; Gabel, Rolf-Dieter; Woog, Heinrich
PATENT ASSIGNEE(S): Boehringer Mannheim Gmbh, Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19615812	A1	19971023	DE 1996-19615812	19960420
ZA 9703331	A	19981019	ZA 1997-3331	19970418
CA 2251886	AA	19971030	CA 1997-2251886	19970421

WO 9739755	A1	19971030	WO 1997-EP1940	19970421
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9726382	A1	19971112	AU 1997-26382	19970421
AU 722516	B2	20000803		
CN 1222079	A	19990707	CN 1997-195629	19970421
BR 9708785	A	19990803	BR 1997-8785	19970421
EP 936913	A1	19990825	EP 1997-918146	19970421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
NZ 332314	A	20000327	NZ 1997-332314	19970421
JP 2000508673	T2	20000711	JP 1997-537711	19970421
RU 2193881	C2	20021210	RU 1998-120909	19970421
NO 9804881	A	19981019	NO 1998-4881	19981019
KR 2000010557	A	20000215	KR 1998-708408	19981020
US 6143326	A	20001107	US 1998-147149	19981125
PRIORITY APPLN. INFO.:			DE 1996-19615812 A	19960420
			WO 1997-EP1940 W	19970421

AB Well-tolerated oral dosage forms of diphosphonic acid derivs. comprise a core contg. the active agent, surrounded by an active agent-free shell such that the rate of release of the active agent is independent of the pH of the medium. Thus, a 200-mg core contg. 10.0 mg ibandronate was coated with a film contg. hydroxypropylmethylcellulose 5.1425, TiO2 2.4650, Macrogol 1.5000, and talc 0.8925 mg to prevent irritation to the upper gastrointestinal tract.

L18 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1997:484505 CAPLUS
DOCUMENT NUMBER:	127:166637
TITLE:	Evaluation of cationic polymer-coated nanocapsules as ocular drug carriers
AUTHOR(S):	Calvo, Pilar; Vila-Jato, Jose L.; Alonso, Maria J.
CORPORATE SOURCE:	Departamento Farmacia Tecnologia Farmaceutica, Facultad Farmacia, Santiago Compostela, 15706, Spain
SOURCE:	International Journal of Pharmaceutics (1997), 153(1), 41-50 CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB New **colloidal** systems for ocular application were developed and their capacity for increasing the corneal penetration of drugs investigated. **Chitosan** (CS)-coated and poly-L-lysine (PLL)-coated poly-.epsilon.-caprolactone (PECL) nanocapsules, were designed based on a strategy that combines the features of PECL nanocapsules as ocular carriers with that advantages of a cationic mucoadhesive coating. Using this approach, an improved interaction of the carrier with the neg. charged corneal epithelium was attempted. The cationic PLL was directly adsorbed onto preformed PECL nanocapsule, whereas the cationic CS was included in the nanocapsules formation medium. The CS and PLL coatings conferred to nanocapsules a high pos. surface charge; nevertheless, they did not modify the release profile of the model drug indomethacin from the **colloidal** system. In vivo studies showed that the systems investigated (uncoated, PLL-coated and CS-coated nanocapsules) increased significantly the concn. of indomethacin in the cornea and aq. humor with respect of a com. eye drops. Nevertheless, the ability of PLL-coated and CS-coated nanocapsules of enhancing the ocular penetration of indomethacin was substantially different: The CS coating increased twice, whereas the PLL coating failed to increase the ocular bioavailability of indomethacin when compared to the uncoated particles. Therefore, it is not the pos. surface charge but the specific nature of CS that is responsible for the particularly enhanced uptake of the CS-coated nanocapsules. In addn., the PLL-coated and CS-coated nanocapsules displayed a good ocular tolerance. Thus, the CS-coated nanocapsules represent a useful approach for increasing the ocular bioavailability of drugs.

L18 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1997:230621 CAPLUS
DOCUMENT NUMBER:	126:347222
TITLE:	Development of positively charged **colloidal** drug carriers. **Chitosan**-coated polyester nanocapsules and submicron-emulsions
AUTHOR(S):	Calvo, P.; Remunan-Lopez, C.; Vila-Jato, J. L.;

Alonso, M. J.
CORPORATE SOURCE: Laboratorio Farmacia Galencia, Facultad Farmacia, Santiago de Compostela, 15706, Spain
SOURCE: Colloid and Polymer Science (1997), 275(1), 46-53
CODEN: CPMSB6; ISSN: 0303-402X
PUBLISHER: Steinkopff
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pos. charged **colloidal** drug carriers have shown interesting properties with respect to the neg. charged systems: they have improved stability in the presence of biol. cations and their interaction with neg. charged biol. membranes is facilitated. In the present work, a new approach to provide a pos. charge to **colloidal** systems, i.e., poly-.epsilon.- caprolactone (PECL) nanocapsules and submicron emulsions, is presented. This is based on the coating of the **colloidal** droplets with the cationic polysaccharide **chitosan** (CS). An exptl. factorial design 33 was used to investigate the influence of several factors (CS viscosity, PECL concn., and lecithin concn.) on the physicochem. properties of the systems. All the formulations displayed a particle size in the nanometer range (200-500 nm) and a high pos. surface charge (from +30 up to +60 mV). The statistical anal. of these data (surface response methodol.) indicated that both size and surface charge of the nanocapsules and submicron emulsions, were significantly affected by all factors under investigation, the CS viscosity being the most relevant factor. The CS coating of the nanocapsules was found to be efficient in preventing their destabilization in the presence of Ca2+. Furthermore, the presence of CS permitted the adequate dispersion of the nano-capsules upon freeze-drying. Finally, using diazepam as model drug, it was obsd. that the encapsulation efficiency was, in all cases, higher than 90% irresp. of the presence of CS in the prepn. As expected, the diazepam release rate from the nanocapsules and submicron emulsions occurred rapidly and it was slightly slowed down due to the CS coating. These results clearly demonstrated that coating nano-capsules and submicron emulsion with CS increases their potential use as **drug delivery** systems.

L18 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:61339 CAPLUS
DOCUMENT NUMBER: 126:79916
TITLE: Stabilization of **colloidal** systems by the formation of ionic lipid-polysaccharide complexes
INVENTOR(S): Alonso Fernandez, Maria Jose; Calvo Salve, Pilar; Remunan Lopez, Carmen; Vila Jato, Jose Luis
PATENT ASSIGNEE(S): Universidade De Santiago De Compostela, Spain; Alonso Fernandez, Maria Jose; Calvo Salve, Pilar; Remunan Lopez, Carmen; Vila Jato, Jose Luis
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9637232	A1	19961128	WO 1996-ES116	19960524
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ES 2093562	A1	19961216	ES 1995-1035	19950526
ES 2093562	B1	19970701		
CA 2195881	AA	19961128	CA 1996-2195881	19960524
EP 771566	A1	19970507	EP 1996-914215	19960524
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, PT, SE				
US 5843509	A	19981201	US 1997-776507	19970227
PRIORITY APPLN. INFO.:			ES 1995-1035	19950526
			WO 1996-ES116	19960524

AB Stabilization of **colloidals** systems occurs through the formation of ionic lipid-polysaccharide complexes. There is disclosed a process for the prepn. of **colloidal** systems which includes the incorporation of a water sol. and pos. charged amino polysaccharide and a neg. charged phospholipid. The **colloidal** systems (which comprise polymer nanoparticles, nanocapsules and nano-emulsions) are stabilized through the formation of a ionic complex, at the interface, comprised of the aminopolysaccharide and the phospholipid. The **colloidal** systems are characterized in that have a particle size lower than 1 .mu.m, an elec. pos. charge and an exceptional stability during storage. They are lyophilizable so that they can be dry stored and redispersed subsequently while maintaining the original characteristics of the system. They are useful as pharmaceutical forms for the oral, transdermic, topical, ocular, nasal and vaginal administration of medicaments. They are also useful as

forms for cosmetic use.

S.N. 10/069,400

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(FILE 'HOME' ENTERED AT 09:57:42 ON 06 MAY 2003)

FILE 'CAPLUS' ENTERED AT 09:57:54 ON 06 MAY 2003
             E HOFFMANN HANS/IN,AU
L1         113 S E3-4 OR E29-30
             E ASMUSSENBODO/IN,AU
             E ASMUSSEN BODO/IN,AU
L2          83 S E1-4
L3       14181 S CHITOSAN
L4         186 S L1 OR L2
L5           2 S L3 AND L4
L6          53 S NANOSOL OR (NANO SOL)
L7           1 S L4 AND L6
L8           2 S L6 AND L3
L9           1 S L8 NOT L5
L10      62823 S COLLOID
L11      95626 S COLLOIDAL
L12     137145 S L10 OR L11
L13        316 S L12 AND L3
L14     796635 S SOLUBLE OR SOLUBILIZ? OR SOLUBILITY
L15         68 S L14 AND L13
L16          1 S 2001:150590/AN
L17      86430 S DRUG DELIVERY
L18         36 S L13 AND L17
L19       1951 S L3 AND L14
L20        254 S L19 AND L17
L21        254 S L3 AND L14 AND L17
L22        242 S L21 NOT L18
L23     545740 S SOL
L24      12153 S ZWITTERION?
L25      16608 S AMPHIPHIL?
L26     609609 S CHARG?
L27     229019 S IONIC
L28    1355992 S L23 OR L24 OR L25 OR L26 OR L27
L29         177 S L22 AND L28
L30        1728 S COACERVATION
L31           4 S L29 AND L30
L32         173 S L29 NOT L31
L33     610336 S DNA
L34         569 S NANOPARTICULATE
L35          13 S L32 AND (L33 OR L34)
L36         160 S L32 NOT L35
L37       22534 S NANOPARTICLE
L38           6 S L37 AND L36
L39         160 S L36 NOT LL38
L40         154 S L36 NOT L38
L41       11670 S L3/AB
L42          97 S L41 AND L40
L43       14746 S HYDROGEL
L44          12 S L42 AND L43
L45          85 S L42 NOT L44
L46      831420 S PEPTIDE OR (AMINO ACID)
L47          21 S L45 AND L46
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L31 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:300871 CAPLUS
TITLE: Uniform polymer films for rapid dissolve dosage form incorporating taste-masking compositions
INVENTOR(S): Fuisz, Richard C.; Yang, Robert K.; Myers, Gary L.
PATENT ASSIGNEE(S): Kosmos Pharma, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003030883	A1	20030417	WO 2002-US32594	20021011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-328868P P 20011012
US 2002-74272 A 20020214
US 2002-386937P P 20020607
US 2002-414276P P 20020927

AB A thin film **drug delivery** compn. includes (i) a flowable water-**sol**. film forming polymeric matrix; (ii) a particulate bioeffecting agent uniformly stationed therein; and (iii) a taste-masking agent coated or intimately assocd. with the particulate to provide taste-masking of the bioeffecting agent. The combined particulate and taste-masking agent have a particle size of 200 .mu. or less and the flowable water-**sol**. film forming matrix is capable of being dried without loss of uniformity in the stationing of the particulate bioeffecting agent therein. The combined particulate and taste-masking agent have a particle size of 150 .mu. or less, for example 100 .mu. or less. Moreover, the flowable water-**sol**. film forming matrix is formable into a dry film of less than about 380 .mu. in thickness, for example less than about 250 .mu. in thickness. For example, a film compn. was prepd. contg. hydroxypropyl Me cellulose 15.6, corn starch 10.41, polyvinylpyrrolidone 10.41, xanthan gum 1.14, Cremophor EL 2.0, propylene glycol 11.67, silicone emulsion anti-foam agent 2.44, spearmint flavor 10.43, loratadine 16.62, and sweetener 9.36 parts, resp.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:187887 CAPLUS
DOCUMENT NUMBER: 138:226735
TITLE: Microcapsules containing enteric-**soluble** anionic cellulose derivatives and cationic crosslinking polymers and their manufacture
INVENTOR(S): Tanno, Fumie; Hayakawa, Kazuhisa
PATENT ASSIGNEE(S): Shin-Etsu Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003070881	A2	20030311	JP 2001-271155	20010907

PRIORITY APPLN. INFO.: JP 2001-271155 20010907

AB In the microcapsules contg. core materials, enteric-**sol**. anionic cellulose derivs., and cationic polymers as crosslinking polymers, the capsule walls are manufd. by mixing (a) alk. soln. of the anionic cellulose derivs. showing pH near their dissoln. point with (b) acidic soln. of the cationic crosslinking polymers through **coacervation** (phase sepn.). The method can be applied to both water-**sol**. core materials and fat-**sol**. core materials and the microcapsules show pH-dependent dissoln. in artificial enteric juice. Aq. soln. (pH 5.3) contg. HP 55S (hydroxypropyl Me cellulose phthalate) and NaOH and Disparlure [(.+-.)-cis-7,8-epoxy-2-methyloctadecane] were gradually added

dropwise through double orifice into AcOH soln. contg. **chitosan** and NaCl under stirring at 5.degree.. The reaction mixt. was filtered and the filter residue was dried to give microcapsules.

L31 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:888625 CAPLUS
DOCUMENT NUMBER: 137:389142
TITLE: Vegetable protein-based microcapsules
INVENTOR(S): Richard, Joeel; Morteau, Sophie
PATENT ASSIGNEE(S): Mainelab, Fr.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092217	A1	20021121	WO 2002-FR1652	20020516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2824756	A1	20021122	FR 2001-6441	20010516

PRIORITY APPLN. INFO.: FR 2001-6441 A 20010516

AB The invention relates to a method of producing microcapsules contg. a material to be encapsulated. Said method is characterized in that a mixt. of at least one **solubilized** vegetable protein and a polyelectrolyte with an opposite **charge** to the protein is subjected to complex **coacervation** in an aq. medium, possibly followed by hardening, in the presence of said material to be encapsulated.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:181646 CAPLUS
DOCUMENT NUMBER: 128:235081
TITLE: Site-specific **drug delivery** using **chitosan** microparticles
AUTHOR(S): Remunan-Lopez, C.; Lorenzo, M. L.; Portero, A.; Jato, J. L. Vila; Alonso, M. J.
CORPORATE SOURCE: Dep. Pharm. Pharm. Technol., Fac. Pharm., Univ. Santiago de Compostela, Santiago de Compstela, 15706, Spain
SOURCE: Advances in Chitin Science (1997), 2, 600-607
CODEN: ACSCFF
PUBLISHER: Jacques Andre
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Chitosan** (CS) is gaining increasing importance in the field of drug controlled release owing to its good biocompatibility, non-toxicity and biodegradability. Recently, CS has also been shown to have mucoadhesive properties and to enhance the penetration of macromols. across the intestinal and nasal barriers. These properties have encouraged greater prospects for its use in the oral and nasal administration of proteins and peptides. Furthermore, CS has been found to be a promising carrier for colon-specific **drug delivery**. From a technol. point of view, CS has unique properties which makes it an excellent material in microencapsulation technologies. In spite of this, only a few articles on this specific area have been published so far. Four main approaches have been proposed for the prepn. of CS microparticles: (1) ionotropic gelation with an opposite **charged** polyelectrolyte, such as sodium tripolyphosphate or alginate, (2) simple or complex **coacervation**, (iii) spray-drying and (i.v.) solvent evapn. The main limitation to all these procedures is that the microspheres obtained are unable to control the release of the microencapsulated compd. after their oral administration. The authors' objective was to develop two new types of microparticulate controlled release systems based on CS to achieve site-specific delivery of drugs following oral administration. With both systems, our aim was to overcome the problem due to the high **soly**. of CS in the acidic pH of the stomach while avoiding chem. crosslinking with aldehydes.

L35 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:716321 CAPLUS
DOCUMENT NUMBER: 137:246527
TITLE: Multivalent MHC constructs: Immunoanalysis, diagnosis and therapy
INVENTOR(S): Winther, Lars; Petersen, Lars Oestergaard; Buus, Soeren; Schoeller, Joergen; Ruub, Erik; Aamellem, Oeystein
PATENT ASSIGNEE(S): Dako A/S, Den.; Dynal Biotech Asa
SOURCE: PCT Int. Appl., 304 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072631	A2	20020919	WO 2002-DK169	20020313
WO 2002072631	C1	20021128		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DK 2001-435	A	20010314
DK 2001-436	A	20010314
DK 2001-441	A	20010314
US 2001-275447P	P	20010314
US 2001-275448P	P	20010314
US 2001-275470P	P	20010314

AB The authors disclose MHC mol. constructs (classical and non-classical) conjugated to sol. or insol. carriers wherein the affinity and avidity of the constructs exceed that of comparable MHC tetramers. In one example, the construct is comprised of biotinylated HLA-A2 bound to FITC-labeled streptavidin conjugated to sol. derivatized dextran. The above construct loaded with MART-1 or influenza virus peptides was shown to effect T-cell activation at a lower concn. than. Also comprised by the present invention is the sample-mounted use of MHC mols., MHC mol. multimers, and MHC mol. constructs.

L35 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:555628 CAPLUS
DOCUMENT NUMBER: 137:114498
TITLE: Nucleic acid delivery formulations
INVENTOR(S): Barman, Shikha P.; Roy, Krishnendu; Hedley, Mary Lynne; Wang, Daqing
PATENT ASSIGNEE(S): Zycos Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057424	A2	20020725	WO 2002-US1379	20020117
WO 2002057424	A3	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-262219P	P	20010117
US 2001-270256P	P	20010220
US 2001-300484P	P	20010622

AB The invention is based on the discovery that injectable and nucleic acid-compatible polymeric compns. and formulations can be structurally designed to regulate nucleic acid activity or gene expression in vivo, for

example, by controlling the bioavailability of the nucleic acid via modulation of the biodegradability and crosslink d. of the network formed by the components of the formulation. The polymeric network encases the nucleic acid, not only controlling the release of the **DNA**, but also providing protection from degrdn. The invention described herein improves upon prior modes of gene delivery, in that gene expression can be regulated by modulation of a polymeric network formed by combination of at least two water-**sol**. components capable of reacting with one another. The nucleic acid of interest is incorporated into the network to be released in a sustained manner to achieve level and duration of activity or expression needed.

L35 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:504596 CAPLUS
DOCUMENT NUMBER: 137:68184
TITLE: pH-sensitive mucoadhesive film-forming gels and wax-film composites for topical and mucosal delivery of pharmaceuticals
INVENTOR(S): Mumper, Russell; Jay, Michael
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051382	A2	20020704	WO 2001-US49524	20011227
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002142042	A1	20021003	US 2000-748133	20001227
US 2002132008	A1	20020919	US 2002-72320	20020207

PRIORITY APPLN. INFO.: US 2000-748133 A1 20001227

AB The present invention relates to pH-sensitive mucoadhesive film-forming gels and wax-film composites suitable for topical and mucosal delivery of pharmaceuticals. The gels comprise a pharmaceutically acceptable pH-sensitive polymer that responds to a lowering of pH by pptg. into films when in contact with the skin or mucosal surface. The films also comprise an adhesive polymer that allows the film to remain in contact with the tissue for an extended period of time. The wax-film composites comprise a bi-layer film having both the pH-sensitive mucoadhesive layer to promote strong adherence to the skin and mucosal surfaces as well as a specially bonded wax layer intended to extend the adherence of the film to tissues for a prolonged period of time. The invention also relates to the use of the pH-sensitive film-forming gels and wax-film composites to deliver peptides, proteins, and nucleic acids either locally to act at the site of administration or for the absorption of the mols. across biol. membranes into the systemic circulation. A 5% triclosan pH-sensitive mucoadhesive film-forming gel suspension was made as follows. Noveon (0.5%) and Carbomer 971 (0.65%)were added very slowly to water (39.0%) with stirring until the soln. was clear and viscous with no visible solid material in soln. Glycerin (50.6 g) was then added to the polymers in water. Eudragit L100 (2.0%) was added and the soln. and the viscous soln. became slightly milky in color and less viscous. NaOH (2.4%) was then added and the whitish gel became viscous. Triclosan (5.0%) was then added to produce a homogeneous whitish gel suspension. The pH of the gel was 6.5. When the 5% triclosan gel was spread onto the skin of a human volunteer hand, it produced a clear film. The 5% triclosan gel was stable when stored under the conditions tested.

L35 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:487335 CAPLUS
DOCUMENT NUMBER: 137:68153
TITLE: Novel in-situ forming polymer-based controlled release microcarrier delivery systems
INVENTOR(S): Bhagwatwar, Harshal Prabhakar; Bapat, Varada Ramesh; Paithankar, Mahesh Balkrishna; Yeola, Bhushan Subhash; Gosavi, Arun Shriniwas; Bagool, Manoj Anil; Shetty, Nitin; Shukla, Milind Chintaman; De Souza, Noel John; Khorakiwala, Habil Fakhruddin

PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049573	A2	20020627	WO 2001-IN219	20011214
WO 2002049573	A3	20030130		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003049320	A1	20030313	US 2001-23427	20011212
AU 2002022505	A5	20020701	AU 2002-22505	20011214

PRIORITY APPLN. INFO.: US 2000-256319P P 20001218
WO 2001-IN219 W 20011214

AB A ready-to use, stable, gelled polymer droplet-in-oil dispersion is described which helps in in-situ formation of a multitude of small solid, semisolid, or gelled microcarriers. The dispersion is placed into a body in a semisolid form and cures to form the delivery system in-situ. The process for making such a dispersion comprises the steps of (i) dissolving a polymer in a biocompatible solvent at an elevated temp. to form a polymer soln., (ii) prepg. a second oil phase soln. of a biocompatible emulsifier at an elevated temp., (iii) mixing the polymer soln. with the oil phase soln. at an elevated temp. and subsequently cooling to refrigeration temp. Placing the gelled dispersion within a body produces the microcarrier delivery system in-situ. The compn. of a syringeable, biodegradable dispersion incorporating an effective level of a biol. active agent before injection into a body provides a novel controlled delivery system of drugs for health-care applications. Thus, Poly(DL-lactide-co-glycolide) was dissolved in DMSO to form a polymer soln. of a 30% wt./wt. concn. To this soln. was added leuprolide acetate to form a 10% wt./wt. soln. of the drug with respect to the polymer. The polymer soln. was injected by into a continuous oil phase comprising a 20% wt./wt. soln. of sorbitan monostearate (Arlacel 60) in super refined sesame seed oil maintained at 70-75.degree., accompanied by high speed homogenization at 13,000 rpm, for 3 min. The resulting polymer droplet-in-oil dispersion was cooled to room temp. with continuous mixing to obtain an opaque mass with a gel-like consistency, which did not flow. The gel was stored under refrigerated conditions until further use. The gel was smooth to the touch with an absence of any gritty particles. Microscopic observation of the gel revealed discrete distorted blue colored droplets of the discontinuous phase dispersed within the continuous oil phase.

L35 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:366800 CAPLUS
DOCUMENT NUMBER: 138:126853
TITLE: Water-based **nanoparticulate** polymeric system for protein delivery: permeability control and vaccine application
AUTHOR(S): Prokop, Ales; Kozlov, Evgenii; Newman, Gale W.; Newman, Mark J.
CORPORATE SOURCE: Chemical Engineering Department, Vanderbilt University, Nashville, TN, 37235, USA
SOURCE: Biotechnology and Bioengineering (2002), 78(4), 459-466
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The idea of using polymeric nanoparticles as drug carriers is receiving an increasing amt. of attention both in academia and industry, Nanoparticles have a no. of potential applications in protein, drug and vaccine delivery, as well as gene therapy applications. In this article, we focus on this unique **drug delivery** technol. as a method to control the release rate of substances, not only for protein delivery but also for delivering an exptl. vaccine immunogen. Nanoparticles were assembled on the basis of **ionic** interaction between water-sol. polymers so that the resulting particles were stable in physiol. media. Among the typical polymers used to assemble

nanoparticles, different polysaccharides, natural amines, and polyamines were investigated. The entrapped substances tested included a protein and antigens. Polydextran aldehyde was incorporated into the particle core, to enable physiol. crosslinking as a method to control permeability. This resulted in long-term retention of substances that would otherwise rapidly leak out of the nanoparticles. Results of crosslinking expts. clearly demonstrated that the release rate could be substantially reduced, depending on the degree of crosslinking. For vaccine antigen delivery tests, we measured an antibody prodn. after s.c. and oral administration. The data indicated that only the crosslinked antigen was immunogenic when the oral route of administration was used. The data presented in this article address primarily the utility of **nanoparticulates** for oral delivery of vaccine antigen.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:701741 CAPLUS
DOCUMENT NUMBER: 137:52155
TITLE: Galactosylated **chitosan**-graft-poly(ethylene glycol) as hepatocyte-targeting **DNA** carrier
AUTHOR(S): Park, I. K.; Kim, T. H.; Park, Y. H.; Shin, B. A.; Choi, E. S.; Chowdhury, E. H.; Akaike, T.; Cho, C. S.
CORPORATE SOURCE: Seoul National University, School of Agricultural Biotechnology, Suwon, 441-744, S. Korea
SOURCE: Journal of Controlled Release (2001), 76(3), 349-362
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lactobionic acid bearing galactose group was coupled with **chitosan** for liver specificity, and poly(ethylene glycol) (PEG) was grafted to galactosylated **chitosan** (GC) for stability in water and enhanced cell permeability. Complex formation of galactosylated **chitosan** -graft-PEG (GCP)/**DNA** complexes was confirmed by agarose gel electrophoresis. Compared to GC/**DNA** complex, the stability of GCP/**DNA** complex could be enhanced. Particle sizes of GCP/ **DNA** complexes decreased as the **charge** ratio of GCP to **DNA** increased and had a min. value around 27 nm at the **charge** ratio of 5. Conformational change of **DNA** did not occur after complex formation with GCP compared to conformation of **DNA** itself. GCP/**DNA** complexes were only transfected into Hep G2 having a sialoglycoprotein receptors, indicative of specific interaction of ASGR on cells and galactose ligands on GCP.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:494396 CAPLUS
DOCUMENT NUMBER: 135:376625
TITLE: Water-**soluble** and low molecular weight **chitosan**-based plasmid **DNA** delivery
AUTHOR(S): Lee, Minhyung; Nah, Jae-Woon; Kwon, Youngmin; Koh, Jae Joon; Ko, Kyung Soo; Kim, Sung Wan
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry, Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112-5820, USA
SOURCE: Pharmaceutical Research (2001), 18(4), 427-431
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Chitosan**, a natural cationic polysaccharide, is a candidate non-viral vector for gene delivery because of its high pos. **charges** and low cytotoxicity. In this study, low mol. wt. **chitosan** (LMWC, mol. wt. of 22 kDa) was characterized and evaluated as a gene carrier. Plasmid/LMWC complex was analyzed in 1% agarose gel electrophoresis. To confirm that the LMWC protected plasmids from nuclease, DNase I protection assays were performed. PSV-.beta.-galactosidase plasmid/LMWC complex was transfected into 293T cells and transfection efficiency was evaluated by .beta.-galactosidase assay. Cytotoxicity of LMWC was detd. by MTT assay. Unlike high mol. wt. **chitosan** (HMWC), LMWC is highly water **sol.**, and can form complex with plasmids in physiol. buffer. The plasmid **DNA** was completely retarded at a wt. ratio of 1:2 (plasmid:LMWC) in 1% agarose gel. DNase I protection assay showed that plasmids were protected from DNase I over 60 min. The most efficient transfection was obtained at a wt. ratio of 1:3 (plasmid:LMWC). The transfection efficiency of LMWC was significantly higher than naked **DNA** and higher than

poly-L-lysine (PLL). MTT assay showed that LMWC was less cytotoxic than PLL. LMWC is non-toxic and has higher transfection efficiency than PLL. Therefore, LMWC will be useful in the development of safe gene carriers.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:489907 CAPLUS
DOCUMENT NUMBER: 135:81959
TITLE: Gene transfer to intervertebral disc cells, and use in the treatment of degenerative disk disorders, and animal model for degenerative disk disease
INVENTOR(S): Kang, James D.; Evans, Christopher H.; Nishida, Kotaro; Robbins, Paul D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001006948	A1	20010705	US 1998-199978	19981125

PRIORITY APPLN. INFO.: US 1998-199978 19981125

AB Methods for transferring a gene to an intervertebral disk are disclosed. The methods find application in the treatment of patients for degenerative disk disorders, by use of a gene encoding a product that imparts a therapeutic and/or prophylactic benefit. The methods also find application in the establishment of an animal model for the study of degenerative disk disease. A genetically modified intervertebral disk cell is also disclosed.

L35 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:489214 CAPLUS
DOCUMENT NUMBER: 135:82005
TITLE: **Drug delivery** system based on multicomponent water-**soluble** polymers exhibiting permeability control
INVENTOR(S): Prokop, Ales
PATENT ASSIGNEE(S): Nanodelivery, Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047501	A1	20010705	WO 2000-US35587	20001229
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002034552	A1	20020321	US 2000-752056	20001229
US 6482439	B2	20021119		
US 2003035838	A1	20030220	US 2002-256508	20020927

PRIORITY APPLN. INFO.: US 1999-173503P P 19991229
US 2000-752056 A3 20001229

AB Microparticles and nanoparticles prepd. from oppositely **charged** polymers are provided in which a drug is incorporated into the core and is conjugated to one polymer by a Schiff-base crosslink. The particles are suitable for use in injectable formulations in which the rate of release of the drug through the particle shell is slowed as compared to non-crosslinked drugs. Enzymically degradable polymers can be incorporated in otherwise hydrolytically stable particles to provide drug release at particular sites within the body where the enzyme of interest is present. For example, crosslinked protein-loaded nanoparticles were prepd. from (i) a droplet-forming polyanionic soln. composed of high-viscosity sodium alginate, cellulose sulfate, a protein (ovalbumin), and dextran polyaldehyde (PDA), and (ii) a corona-forming polycationic soln. composed of spermine hydrochloride, poly(methylene-co-guanidine)

hydrochloride, CaCl2, and Pluronic F 68. The Schiff-base product between the anionic groups of ovalbumin and aldehyde group of PDA allowed an adjustment of release via ion exchange as opposed to no release for permanently bound ovalbumin.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:300486 CAPLUS
DOCUMENT NUMBER: 134:331616
TITLE: Sustained release microspheres based on a carrier protein, a water soluble polymer and complexing agents
INVENTOR(S): Scott, Terrence L.; Brown, Larry R.; Riske, Frank J.; Blizzard, Charles D.; Rashba-Step, Julia
PATENT ASSIGNEE(S): Epic Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028524	A1	20010426	WO 2000-US28200	20001012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6458387	B1	20021001	US 1999-420361	19991018
EP 1223917	A1	20020724	EP 2000-973477	20001012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2003059474	A1	20030327	US 2002-245776	20020917

PRIORITY APPLN. INFO.: US 1999-420361 A 19991018
WO 2000-US28200 W 20001012

AB A microsphere compn. for sustained release of therapeutic or diagnostic agents comprises (1) a carrier protein, (2) a water-sol. polymer, (3) a polyanionic polysaccharide as a first complexing agent, and (4) a divalent metal cation (Ca and Mg) as a second complexing agent. The microspheres have a smooth surface that includes a plurality of channel openings that are < 1000 .ANG. in diam. Various drugs were encapsulated into microspheres. For example, microspheres contg. leuprolide acetate were prepd. using human serum albumin (HSA), dextran sulfate, polyethylene glycol, and polyvinylpyrrolidone. The microspheres were composed of approx. 10% leuprolide acetate, 50% human serum albumin, 20% dextran sulfate and 20% polyethylene glycol/polyvinylpyrrolidone. Similar particles were prepd. which also included zinc sulfate or caprylic acid, both of which retarded the release of protein and peptide from the microspheres. Also, rifampicin-contg. HSA microspheres were prepd. with HSA incorporation of 74% and rifampicin incorporation into the particles of > 6.8%. The av. size of the particles was detd. to be 68 nm in diam.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:900214 CAPLUS
DOCUMENT NUMBER: 134:46804
TITLE: Sustained release microspheres comprising macromolecules and water-soluble polymers
INVENTOR(S): Scott, Terence L.; Brown, Larry R.; Riske, Frank J.; Blizzard, Charles D.; Rashba-Step, Julia
PATENT ASSIGNEE(S): Epic Therapeutics, Inc., USA
SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1060741	A1	20001220	EP 1999-304616	19990614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: EP 1999-304616 19990614
AB Methods for forming sustained release microspheres and the products produced thereby are provided. The microspheres have a smooth surface that includes a plurality of channel openings that are less than 1000 .ANG. in diam. The microspheres comprise (1) a macromol. such as a protein and nucleic acid, (2) .gtoreq. 1 water-sol. polymers such as starch, PEG, and PVP, and (3) a complexing agent, which is capable of interacting with a therapeutic agent to facilitate loading, retaining, and/or otherwise delaying the release of the therapeutic agent from the microspheres. Carbonyldiimidazole was added to a soln. of rifampicin in DMF. To the mixt. was added a mixt. of human serum albumin and deionized water. A polymer soln. contg. PVP and PEG in NaOAc soln. was added to the mixt. and the resulting mixt. was incubated and cooled. Particles were isolated and resuspended in water. The av. size of the particles were detd. to be 68 nm in diam.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:89987 CAPLUS
DOCUMENT NUMBER: 130:257276
TITLE: Stability of **chitosan** and poly-L-lysine membranes coating **DNA**-alginate beads when exposed to hydrolytic enzymes
AUTHOR(S): Quong, D.; Yeo, J.-N.; Neufeld, R. J.
CORPORATE SOURCE: Department of Chemical Engineering, McGill University, Montreal, QC, H3A 2A7, Can.
SOURCE: Journal of Microencapsulation (1999), 16(1), 73-82
CODEN: JOMIEF; ISSN: 0265-2048
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Sol. chitosan** and poly-L-lysine are readily hydrolyzed using lysozyme or chitosanase for **chitosan**, and trypsin, chymotrypsin or proteinase K for poly-L-lysine. For similar amts. of enzyme, chitosanase hydrolyzed 57% of the **chitosan**, compared to 35% for lysozyme. In the case of poly-L-lysine, chymotrypsin and trypsin exhibited similar activities, hydrolyzing approx. 41% of the polymer compared to proteinase K at only 16%. In contrast, **chitosan** and poly-L-lysine membranes, coating alginate beads, were almost totally inert to the resp. hydrolytic enzymes. Less than 2% of the membrane wt. was hydrolyzed. It appears that either membrane material would be stable for in vivo application, and in particular in the protection of **DNA** during gastro-intestinal transit. At chitosanase concns. of 1.4mg/mL and in the presence of sodium ions, 20% of the total double-stranded **DNA** was released from **chitosan** coated beads. An exchange of calcium for sodium within the bead liquefied the alginate core releasing **DNA**. The presence of calcium stabilized the alginate bead, retaining all the **DNA**. Highly pure **DNA** was recovered from beads through mech. membrane disruption, core liquefaction in citrate and use of **DNA** spin-columns to sep. **DNA** /alginate mixts. in a citrate buffer. **DNA** recovery efficiencies as high as 94% were achieved when the initial alginate/**DNA** wt. ratio was 1000.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:500209 CAPLUS
DOCUMENT NUMBER: 127:113361
TITLE: Vaccine compositions for intranasal administration containing **chitosan** as adjuvant
INVENTOR(S): Illum, Lisbeth
PATENT ASSIGNEE(S): Danbiosyst UK Limited, UK; Illum, Lisbeth
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720576	A1	19970612	WO 1996-GB3019	19961209

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2237529	AA	19970612	CA 1996-2237529	19961209
AU 9711025	A1	19970627	AU 1997-11025	19961209
AU 705452	B2	19990520		
GB 2322801	A1	19980909	GB 1998-11810	19961209
GB 2322801	B2	20000119		
EP 865297	A1	19980923	EP 1996-941743	19961209
EP 865297	B1	20021106		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2000501412	T2	20000208	JP 1997-521094	19961209
AT 227134	E	20021115	AT 1996-941743	19961209
US 6391318	B1	20020521	US 1998-88185	19980601
NO 9802497	A	19980602	NO 1998-2497	19980602
US 2003039665	A1	20030227	US 2002-141312	20020508

PRIORITY APPLN. INFO.:

GB 1995-25083	A	19951207
WO 1996-GB3019	W	19961209
US 1998-88185	A3	19980601

AB **Chitosan**, administered intranasally together with antigen in vaccines, enhances the immune response to the antigen. Intranasal administration of such vaccines enhances both the protective IgA mucosal immune response and the systemic IgG immune response. The **chitosan** is preferably water **sol**. and 70-95% deacetylated. Thus, an intranasal vaccine soln. was prepd. contg. 0.5% **chitosan** glutamate (11% acetylated), 0.8% NaCl, 0.05% influenza purified surface antigen, and phosphate buffer (pH 6).

L38 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:241781 CAPLUS
DOCUMENT NUMBER: 138:260459
TITLE: Preparation of submicron sized **nanoparticles** via dispersion lyophilization
INVENTOR(S): Brynjelsen, Sean; Doty, Mark; Kipp, James E.; Jayswal, Nailesh; Narayanan, Krishnaswamy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 964,273.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003059472	A1	20030327	US 2002-183035	20020626
WO 2003026611	A2	20030403	WO 2002-US30447	20020925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: US 2001-964273 A2 20010926
US 2002-183035 A 20020626

AB The present invention relates to a process for prepg. submicron sized **nanoparticles** of a poorly water **sol**. compd. by lyophilizing a dispersion or microdispersion of a multiphase system having an org. phase and an aq. phase, the org. phase having the poorly water **sol**. org. compd. therein. The method is preferably used to prep. **nanoparticles** of a poorly water **sol**., pharmaceutically active compd. suitable for in vivo delivery, particularly by parenteral routes.

L38 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:71873 CAPLUS
DOCUMENT NUMBER: 136:123671
TITLE: Ophthalmic formulation of a selective cyclooxygenase-2 inhibitory drug
INVENTOR(S): Kararli, Tugrul T.; Bandyopadhyay, Rebanta; Singh, Satish K.; Hawley, Leslie C.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005815	A1	20020124	WO 2001-US22061	20010712

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002035264	A1	20020321	US 2001-904098	20010712
EP 1303271	A1	20030423	EP 2001-953462	20010712

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-218101P P 20000713
US 2001-279285P P 20010328
US 2001-294838P P 20010531
US 2001-296388P P 20010606
WO 2001-US22061 W 20010712

OTHER SOURCE(S): MARPAT 136:123671

AB A pharmaceutical compn. suitable for topical administration to an eye contains a selective COX-2 inhibitor or **nanoparticles** of a drug of low water **soly**., at a concn. effective for the treatment

and/or prophylaxis of a disorder in the eye, and 1 or more ophthalmically acceptable excipients that reduce rate of removal from the eye such that the compn. has an effective residence time of 2-24 h. Also provided is a method of treating and/or preventing a disorder in an eye, the method comprising administering to the eye a compn. of the invention. Thus, an ophthalmic **nanoparticle** suspension contained valdecoxib at 2.15 mg/g, 1.2% glycerin, 0.8% EDTA disodium salt, 4.0% Gelcarin GP-379NF, 0.21% SeaSpen PF and 0.82% Povidone.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:229690 CAPLUS
DOCUMENT NUMBER: 133:94413
TITLE: Preparation of PEG-grafted **chitosan** **nanoparticles** as peptide drug carriers
AUTHOR(S): Ohya, Y.; Cai, R.; Nishizawa, H.; Hara, K.; Ouchi, T.
CORPORATE SOURCE: Faculty of Engineering and High Technology Research Center, Kansai University, Suita, 564-8680, Japan
SOURCE: S.T.P. Pharma Sciences (2000), 10(1), 77-82
CODEN: STSSE5; ISSN: 1157-1489
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has recently become very important to develop **drug** **delivery** systems for water-**sol**. natural macromols., such as peptides, proteins and polynucleotides. Polyethylene glycol was found to graft to **chitosan**. PEG-g-**chitosan**, formed **nanoparticles** through intermol. hydrogen bonding in an aq. soln. PEG-g-**chitosan** **nanoparticles** can be expected to incorporate water-**sol**., polar or anionic mols., which can then interact with **chitosan** by hydrogen bonds or electrostatically. We therefore decided to investigate the incorporation of a peptide hormone, insulin, as a model peptide drug into PEG-g-**chitosan** **nanoparticles**. PEG-g-**chitosan** **nanoparticles** incorporated a certain quantity of insulin mols. spontaneously, but this depended on the degree of introduction of PEG chain on **chitosan**. The release rate also depended on the degree of introduction of PEG chain on **chitosan**. The sustained release of insulin from **nanoparticles** was also obsd. PEG-g-**chitosan** **nanoparticles** are can be expected to be applied as delivery vehicles for peptide drugs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:190719 CAPLUS
DOCUMENT NUMBER: 132:227178
TITLE: Emulsifier-free finely dispersed systems of the oil-in-water or water-in-oil type
INVENTOR(S): Gers-Barlag, Heinrich; Mueller, Anja
PATENT ASSIGNEE(S): Beiersdorf Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 987003	A2	20000322	EP 1999-116871	19990906
EP 987003	A3	20011024		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19842767	A1	20000323	DE 1998-19842767	19980918
US 2002068073	A1	20020606	US 1999-389684	19990902
US 6410035	B1	20020625		
JP 2000095639	A2	20000404	JP 1999-260141	19990914
US 2002136747	A1	20020926	US 2002-81618	20020221

PRIORITY APPLN. INFO.: DE 1998-19842767 A 19980918
US 1999-389684 A3 19990902

AB Pickering emulsions for use in cosmetic, deodorant, or dermatol. compns. are described which contain an oil phase, an aq. phase, .gtoreq.1 type of **amphiphilic** **nanoparticles** with a mean particle size <200 nm which are optionally coated and are dispersible in either water or oil, .gtoreq.1 polymeric moisturizer, and .ltoreq.0.5 wt.% emulsifiers. These emulsions, and esp. water-in-oil Pickering emulsions, are extremely stable, do not irritate the skin, and do not produce a dry skin feel. Sunscreens contg. these emulsions provide greater sun protection than

conventional sunscreens. Oil-in-water Pickering emulsions are produced by dispersing the amphiphilic particles first in the aq. phase and then adding the oil phase; water-in-oil Pickering emulsions are produced by first dispersing the particles in the oil phase. The polymeric moisturizer is preferably selected from water-sol., swellable, and gel-forming polysaccharides. Thus, a water-in-oil emulsion contained Eusolex T2000 (TiO2) 6, ZnO 4, T805 (TiO2) 2, silica 0.5, Elfacos C26 (hydroxystearyl hydroxystearate) 2, Abil Wax 2440 (behenoxydimethicone) 5, caprylic/capric triglyceride 5, octyldodecanol 5, butylene glycol caprylate/caprate 10, C12-15-alkyl benzoate 10, dimethicone 3, preservative 0.5, glycerin 3, Fucogel 1000 5, NaCl 1, Natrosol Plus 330CS (cellulose gum) 0.1, and H2O to 100 wt.%.

L38 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:764304 CAPLUS
DOCUMENT NUMBER: 132:10518
TITLE: Nucleation and growth of magnetic metal oxide **nanoparticles** and its use
INVENTOR(S): Margel, Shlomo; Gura, Sigalit
PATENT ASSIGNEE(S): Bar-Ilan University, Israel
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962079	A1	19991202	WO 1999-IL275	19990524
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941613	A1	19991213	AU 1999-41613	19990524
EP 1088315	A1	20010404	EP 1999-925247	19990524
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002517085	T2	20020611	JP 2000-551402	19990524

PRIORITY APPLN. INFO.: US 1998-84726 A 19980526
WO 1999-IL275 W 19990524

AB A method for prepg. **nanoparticles** coated with magnetic metal oxide, comprising the following steps: (a) contacting an aq. soln. contg. a **sol**. polymeric metal chelating agent with one or more **sol**. metal salts providing metal ions, wherein at least one of said metal ions is capable of forming an oxide which is magnetic, said metal ions being in amts. which do not exceed substantially the binding capacity of said chelating agent; (b) causing said metal ions to be present in the oxidn. states required for the formation of the oxide which is magnetic; (c) maintaining the pH of the soln. at the range of at least 7; (d) introducing into the soln. addnl. amts. of said metal salts; (e) causing said addnl. metal ions to be present in the oxidn. states required for the formation of the oxide which is magnetic; (f) maintaining the pH of the soln. at the range of at least 7; (g) successively repeating the operations of steps (d) to (f) as many times as required to obtain monodispersed **nanoparticles** coated with magnetic metal oxide.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:492603 CAPLUS
DOCUMENT NUMBER: 132:139024
TITLE: Preparation of **nanoparticle** of PEG-grafted **chitosan** and its application as a carrier of water-**soluble** drugs
AUTHOR(S): Ohya, Y.; Cai, R.; Nishizawa, H.; Hara, K.; Ouchi, T.
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, 564-8680, Japan
SOURCE: Kichin, Kitosan Kenkyu (1999), 5(2), 198-199
CODEN: KKKEFB; ISSN: 1340-9778
PUBLISHER: Nippon Kichin, Kitosan Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Synthesized poly(ethylene glycol)-grafted **chitosan** (PEG-grafted **chitosan**) was synthesized which formed **nanoparticle** in

aq. soln. by its intermol. hydrogen bonds. The **nanoparticle** is expected to entrap water-**sol**. substances having polar and/or anionic groups by hydrogen bond and electrostatic interaction. In this study, we investigated the entrapment and release behavior of insulin, a peptide hormone, into/from the PEG-grafted **chitosan** **nanoparticle** in aq. soln.

L44 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:565805 CAPLUS
DOCUMENT NUMBER: 138:260217
TITLE: Ion replacement mechanism of alginate-**chitosan**-alginate gels
AUTHOR(S): Chen, Yi-Qing; Sun, Duo-Xian
CORPORATE SOURCE: School of Chemical Engineering and Technology, Tianjin University, Tianjin, 300072, Peop. Rep. China
SOURCE: Wuli Huaxue Xuebao (2002), 18(7), 609-612
CODEN: WHXUEU; ISSN: 1000-6818
PUBLISHER: Beijing Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Alginate-**Chitosan**-Alginate(ACA) ion replacement gels are a novel ion adsorbent and are hopeful to be used to cure human toxicosis metallicus. In this paper, ion replacement mechanism of ACA on Pb2+ was studied. **Sol**-gel phase interface of ion replacement process of ACA was obsd. by optical microscope photo. On the basis of it, mobile boundary model (MBM) was used to describe ion replacement process. The results show that the model has high reliability. Ion replacement process was controlled by intraparticle diffusion control (PDC) (to see Fig. 3). The chelating ion-exchanger D418 and macropore acrylic resin D113 were studied for comparative anal. The results show that ACA ion replacement gels has much faster ion exchange velocity than D418 and D113 resin and the two ion adsorbents have different ion replacement mechanism. Ion replacement of ACA is a **sol**-gel phase transition process.

L44 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:340932 CAPLUS
DOCUMENT NUMBER: 138:158669
TITLE: Biocompatibility of thermosensitive **chitosan**-based **hydrogels**: an in vivo experimental approach to injectable biomaterials
AUTHOR(S): Molinaro, Giuseppe; Leroux, Jean-Christophe; Damas, Jacques; Adam, Albert
CORPORATE SOURCE: Universite de Montreal, Faculte de Pharmacie, Montreal, QC, H3C 3J7, Can.
SOURCE: Biomaterials (2002), 23(13), 2717-2722
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Chitosan**, an amino-polysaccharide obtained from the alk. deacetylation of chitin, presents an interest as a drug vehicle. Indeed, **chitosan** solns. contg. glycerol-2-phosphate (.beta.-GP) undergo **sol**-gel transition at a temp. close to 37.degree., which make them suitable for the parenteral administration of drugs. However, before using these **chitosan** derivs. for biomedical applications, it is important to evaluate their biocompatibility, and particularly to test their inflammatory effects. It was injected in the hindpaw of the rat. (i). four **chitosan**/.beta.-GP solns. tested triggered a non-specific response, with solns. prepd. with **chitosans** of higher deacetylation degrees yielding a lesser inflammatory reaction. (ii). systemic pretreatment of animals with icatibant, apafant and diphenhydramine did not significantly diminish this response. Dexamethasone practically abolished it for all solns. and ketanserine only slightly decreased it in one prepn. at two different times. In conclusion, it appears that a higher degree of deacetylation of the chitin chain is desirable for superior biocompatibility.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:278837 CAPLUS
DOCUMENT NUMBER: 138:29025
TITLE: Buparvaquone mucoadhesive nanosuspension: preparation, optimisation and long-term stability
AUTHOR(S): Muller, R. H.; Jacobs, C.
CORPORATE SOURCE: Department of Pharmaceutics, Biophamraceutics and Biotechnology, Free University of Berlin, Berlin, D-12169, Germany
SOURCE: International Journal of Pharmaceutics (2002), 237(1-2), 151-161
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The poorly **sol**. drug buparvaquone is used in exptl. clinics against the gastrointestinal persisting parasite Cryptosporidium parvum.

It was produced as nanosuspension by high pressure homogenization. Main advantages of nanosuspensions (amongst others) are their increase of satn. soly. and dissoln. velocity, improving the bioavailability of drugs. The buparvaquone nanosuspension had a bulk population of about 600 nm (analyzed by photon correlation spectroscopy (PCS)). The addnl. anal. performed with laser diffraction showed that only a very small content of microparticles occurred, which is, for the special features of nanosuspensions, negligible because they were still below 3 .mu.m. Another feature of nanosuspensions is the adhesion properties to surfaces, e.g. mucosa. To further increase the adhesion time of the buparvaquone nanosuspension to C. parvum, the nanosuspension was formulated with **hydrogels** made from mucoadhesive polymers, e.g. different types of Carbopol.RTM. and **chitosan**. Only a small increase of the particle size of the bulk population occurred directly after the incorporation of buparvaquone nanosuspension into the **hydrogels**. The nanosuspension/**hydrogel** systems were phys. long-term stable over a period of 6 mo as indicated by the unchanged particle sizes.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:168650 CAPLUS
DOCUMENT NUMBER: 138:112221
TITLE: Behavior of alginate gel beads containing **chitosan** salt prepared with water-**soluble** vitamins
AUTHOR(S): Murata, Yoshifumi; Kontani, Yukari; Ohmae, Hiroko; Kawashima, Susumu
CORPORATE SOURCE: Faculty of Pharmaceutical Science, Kanazawa, Japan
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2002), 53(2), 249-251
CODEN: EJPBEL; ISSN: 0939-6411
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Alginate gel beads were prepd. which contained weak acid salts of **chitosan** (Alg-CS) and water-**sol**. vitamins (e.g. ascorbic acid (AS)) and the behavior of the beads, uptake of bile acids was investigated in vitro. The Alg-CS beads rapidly took up bile acid and this phenomenon was obsd. for both **hydrogel** beads and dried beads. About 120 .mu.mol of taurocholic acid was taken up into Alg-CS (1 g) prepd. with orotic acid. Dried Alg-CS is the granule which can be made easily, and keeps the ability of CS salt, and all elements can be taken as a food. Therefore, Alg-CS could serve as a useful dietary agent for the prevention of hyperlipidemia.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:51241 CAPLUS
DOCUMENT NUMBER: 136:90994
TITLE: **Drug delivery** system for poorly water-**soluble** drugs
INVENTOR(S): Chornet, Esteban; Ishizawa, Claudia; Dumitriu, Severian
PATENT ASSIGNEE(S): Kemestrie Inc., Can.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003962	A2	20020117	WO 2001-CA993	20010706
WO 2002003962	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1299089	A2	20030409	EP 2001-951278	20010706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003000073	A	20030306	NO 2003-73	20030107

PRIORITY APPLN. INFO.: US 2000-216627P P 20000707
US 2000-252389P P 20001121
WO 2001-CA993 W 20010706

AB The present invention relates to a method for modifying the **solubilization** rates of poorly water **sol.** drugs, using a **chitosan**-xanthan **hydrogel**. In addn., the present invention relates to a process for the prepn. of **chitosan** -xanthane **hydrogels** as well as for the prepn. of **hydrogels** comprising a poorly water **sol.** drug. To prep. a slow-release rate system, a **chitosan** with a high mol. wt. was selected. The **hydrogel** was prepd. following a 2-step process. In a first step fenofibrate was dissolved in ethanol, which was then added under vigorous stirring to an aq. xanthan soln. At this point, a homogeneous dispersion of the drug was formed. The second step involved the **hydrogel** formation, which was achieved by adding the drug-xanthan dispersion to a high mol. wt. aq. **chitosan** soln. The mixt. was stirred for 2 h and then thoroughly washed with water. The final product, the dried gel, was obtained after freeze-drying. A fenofibrate content in the **hydrogel** of about 40% was detd. The results demonstrated a slow-release dissoln. rate for fenofibrate, independent of pH.

L44 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:211325 CAPLUS
DOCUMENT NUMBER: 135:24585
TITLE: A new approach for targeting to Cryptosporidium parvum using mucoadhesive nanosuspensions: research and applications
AUTHOR(S): Kayser, O.
CORPORATE SOURCE: Freie Universitat Berlin, Institut fur Pharmazie, Pharmazeutische Technologie, Biopharmazie and Biotechnologie, Berlin, 12169, Germany
SOURCE: International Journal of Pharmaceutics (2001), 214(1-2), 83-85
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new strategy to deliver antibiotics to the Cryptosporidium-infected gastrointestinal tract is presented. In an effort to augment the anticryptosporidial effect of clin. used drugs, mucoadhesive nanosuspensions were prepd. They have the ability to reside in the gastrointestinal tract for an extended period. The **hydrogel** contained bupravaquone nanosuspensions and an adhesive polymer (**chitosan**) powder dispersed in water. By the development of mucoadhesive nanosuspensions, a potential **drug delivery** system for poorly **sol.** drugs was investigated to overcome bioavailability problems caused by the pathophysiol. diarrheic situation in patients suffering from cryptosporidiosis. Adapting **drug delivery** systems to the situation of Cryptosporidium parvum infections in men allows increased retention times with a prolonged action at reduced elimination in the gastrointestinal tract. In this communication, in vivo data are presented to document the efficiency of bupravaquone formulated as mucoadhesive polymers to improve its activity against C. parvum.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:175864 CAPLUS
DOCUMENT NUMBER: 132:224040
TITLE: Erodible solid **hydrogels** for delivery of biologically active materials
INVENTOR(S): Uchegbu, Ijeoma Florence
PATENT ASSIGNEE(S): University of Strathclyde, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014155	A1	20000316	WO 1999-GB2960	19990907

W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: GB 1998-19461 19980908

AB A title material, useful for delivery of biol. active materials, e.g.,

pharmaceuticals, is formed from noncovalently crosslinked polysaccharide derivs., which bear both hydrophilic and hydrophobic groups. Gel formation is then induced, e.g., by freeze-drying. The gel is erodible either by simple mech. disruption or due to biol. processes acting on the **hydrogel**. Thus, amidation of H2O-**sol**. glycol **chitosan** with N-hydroxysuccinimidyl palmitate ester gave D2O-insol. (but dispersible) title **hydrogel** which was loaded with Rhodamine B and its release properties examd.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:730579 CAPLUS
DOCUMENT NUMBER: 132:98031
TITLE: A non-covalently crosslinked **chitosan** based **hydrogel**
AUTHOR(S): Noble, L.; Gray, A. I.; Sadiq, L.; Uchegbu, I. F.
CORPORATE SOURCE: Strathclyde Institute for Biomedical Sciences, Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow, UK
SOURCE: International Journal of Pharmaceutics (1999), 192(2), 173-182
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Hydrogels** are normally formed by the covalent crosslinking of linear polymers. In the case of **chitosan** based **hydrogels** this crosslinking is often achieved with glutaraldehyde, glyoxal or other reactive crosslinking agents. Such **hydrogel** materials have limited biocompatibility and biodegradability. However by the attachment of hydrophobic palmitoyl groups to glycol **chitosan**, a water **sol**. **chitosan** deriv., the authors have produced a version of the **amphiphilic** vesicle forming polymer-palmitoyl glycol **chitosan** (Uchegbu et al., 1998, J Pharm Pharmacol 58, 453-458). The level of palmitoylation in this variant of the polymer (GCP11), as detd. by proton neutron magnetic resonance spectroscopy, is 19.62.+-.2.42% (n=4). GCP11 has been used to prep. soft, slowly eroding **hydrogels** suitable for **drug delivery** by simply freeze-drying an aq. dispersion of the polymer. Non-covalent crosslinking to form the gel matrix is achieved by the hydrophobic interactions of the palmitoyl groups. The resulting material, as examd. by SEM, is porous and may be hydrated to up to 20.times. its wt. in aq. media without any appreciable change in vol.-transforming from an opaque to a translucent solid. The slow erosion of this material in aq. environments gives a biodegradable and ultimately more biocompatible material than covalently cross-linked **hydrogels**. Unlike most **chitosan**-based gels, the gel is hydrated to 20.times. its wt. at alk. pH but only 10.times. its wt. at neutral and acid pH. This is as a result of the gradual erosion of the gel at lower pH values. Hydration is also reduced from 20.times. the dry gel wt. in water to 10.times. the dry gel wt. in the presence of dissolved salts such as sodium chloride. GCP11 **hydrogels** have been loaded to 0.1% wt./wt. with a model fluorophore, rhodamine B, by simply freeze-drying an aq. dispersion of GCP11 in the presence of a soln. of rhodamine B dissolved in either water or phosphate buffered saline (PBS, pH=7.4). The release of this model fluorophore was retarded by between 8 and 12% when PBS was contained in the gel in accordance with the hydration profiles. Rhodamine B release was also reduced by between 13 and 25% in the presence of acid as a result of the reduced **soly**. of rhodamine B at acid pH.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:270823 CAPLUS
DOCUMENT NUMBER: 131:49332
TITLE: **Chitosan hydrogel** as a base for transdermal delivery of berberine and its evaluation in rat skin
AUTHOR(S): Tsai, Chia-Jung; Hsu, Li-Ren; Fang, Jia-You; Lin, Hung-Hong
CORPORATE SOURCE: School of Pharmacy, Chia Nan College of Pharmacy and Science, Tainan Hsien, Taiwan
SOURCE: Biological & Pharmaceutical Bulletin (1999), 22(4), 397-401
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Berberine is the main ingredient of Coptis. This study selected berberine

as a model drug to design a transdermal delivery system for the treatment of cutaneous leishmaniasis. Berberine was incorporated into **chitosan hydrogel** to prep. ointments. The physicochem. properties of the ointments and the release profile of berberine were investigated. The viscosity of **chitosan hydrogel** increased with an increasing amt. of lactic acid or EDTA. The effect of EDTA on the viscosity was greater than that of lactic acid. By DSC measurement, no interaction was found to occur between **chitosan** and the **sol**. berberine. The release rate of berberine was inversely proportional to ointment viscosity. In in vitro skin perfusion studies, only trace amts. of berberine permeated through the rat skin due to its low oil-water partition coeff. Surfactants were used as penetration enhancers to increase the percutaneous absorption of berberine. Among the enhancers, benzalkonium chloride was found to be the most efficient. Addnl., Tween 80 could increase the loading amt. of berberine in the skin.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:44997 CAPLUS
DOCUMENT NUMBER: 130:100682
TITLE: Supported polyionic **hydrogels**
INVENTOR(S): Dumitriu, Severian; Guttmann, Hilda; Kahane, Itzhak
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Israel Fiber Institute, State of Israel Ministry & Trade
SOURCE: U.S., 5 pp., Cont.-in-part of U.S. 5,648,252. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858392	A	19990112	US 1997-806218	19970226
IL 109079	A1	19980222	IL 1994-109079	19940322
US 5648252	A	19970715	US 1995-409264	19950322

PRIORITY APPLN. INFO.: IL 1994-109079 19940322
US 1995-409264 19950322

AB A supported polyionic **hydrogel** is prepd. by impregnating a support material with a soln. of anionic polysaccharide and a soln. of cationic polysaccharide where the anionic polysaccharide and cationic polysaccharide react with each other to form a polyionic **hydrogel** impregnated in the support material. The **hydrogel** may be dried such as by lyophilization. Preferably, the anionic polysaccharide is xanthan, dicarboxystarch or dicarboxycellulose and the cationic polysaccharide is **chitosan**. Esp. preferred is a polyionic **hydrogel** formed from xanthan and **chitosan**. A paper material or a textile material can be used as the support material. A dry supported polyionic **hydrogel** can be formed as a bandage without active material incorporated therein. The supported polyionic **hydrogel** may be formed contg. a biol. active material by having the active material in either polysaccharide soln. or in another soln. impregnated into the support material. The biol. active materials can be enzymes, antibody-producing cells or water-**sol**. drugs such as the antimicrobial agent, chlorohexidine. Urease (300 mL) in HED buffer was added to 30 mL of 0.3% xanthan and stirred, then 30 mL of the 0.3% **chitosan** soln., at pH 6.4, were added and the gel formed was stirred for 15 min at room temp. The mixt. was centrifuged for 15 min at 15,000 rpm. The supernatant was removed and the gel washed with 2 mL of the HED buffer. The gel was sepd. by centrifugation and was lyophilized and stored at -20.degree. C. The urease retained its activity in this **hydrogel** after lyophilization and rehydration.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:138239 CAPLUS
DOCUMENT NUMBER: 126:242722
TITLE: **Hydrogel** beads based on amidated pectins for colon-specific **drug delivery**: the role of **chitosan** in modifying drug release
AUTHOR(S): Munjeri, O.; Collett, J. H.; Fell, J. T.
CORPORATE SOURCE: Department of Pharmacy, University of Manchester, Manchester, UK
SOURCE: Journal of Controlled Release (1997), 46(3), 273-278 CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A multiparticulate system with the potential for site-specific delivery to the colon was investigated. Gelation of droplets of amidated pectin solns. in the presence of calcium is the basis of the method of prepn. Two drugs, indomethacin and sulfamethoxazole were successfully incorporated into the beads. Drug release from the beads was a function of media pH and drug loading. In simulated gastric and small intestinal conditions, drug release was greater with the more **sol**. sulfamethoxazole, but release of both drugs was reduced to satisfactory levels by the formation of a **chitosan** polyelectrolyte complex around the beads. All the prepns. released drug in simulated colonic conditions within 135 min.

L44 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:31966 CAPLUS
DOCUMENT NUMBER: 126:108840
TITLE: Sustained-release matrix tablet containing sodium alginate and excipients
AUTHOR(S): Shin, Sung-I.; Lee, Beom-Jin; Lee, Tae-Sub; Heo, Bo-Uk; Ryu, Seung-Goo
CORPORATE SOURCE: College Pharmacy, Kangwon National University, Chuncheon, 200-701, S. Korea
SOURCE: Yakche Hakhoechi (1996), 26(3), 187-192
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB The matrix tablet contg. Na alginate and CaHPO4 releases drugs in a controlled fashion from **hydrogel** with gelling and swelling due to their interaction as water penetrates the matrixes of the tablet. The purpose of this study was to evaluate release characteristics of the matrix tablet varying the amt. of Na alginate, CaHPO4 and other excipients such as **chitosan**, hydroxypropyl Me cellulose (HPMC) and Eudragit RS100 in the simulated gastric and intestinal fluid. The practically **sol**. ibuprofen was used as a model drug. The release profiles of matrix tablet in the gastric fluid as a function of Na alginate/CaHPO4 ratio were not pronounced because of low **soly**. of the drug and stability of alginate matrixes. However, release rate of the drug from the matrix in the intestinal fluid was largely changed when Na alginate/CaHPO4 ratio was increased, suggesting that the ratio of Na alginate/CaHPO4 was an important factor to control the gelling and swelling of the matrix tablet. The incorporation of other excipients into the matrix tablet also influenced the release rate of the drug. The **chitosan** and HPMC decreased the release rate of the drug. No release of the drug was occurred when Eudragit RS100 was added into the tablet. The retarded release of matrix tablet when excipients were added resulted from the hindrance of swelling and gelling of the matrix tablet contg. Na alginate and CaHPO4. The hardness and bulk d. of the matrix tablet were not correlated with release rate of drug in the study. From these findings, the ratio of Na alginate and CaHPO4 in the matrix tablet in addn. to incorporation of excipients could be very important to control the release rate of drug in dosage form design.

L47 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:59341 CAPLUS
DOCUMENT NUMBER: 138:253565
TITLE: Kinetics and mode of **peptide** delivery via the respiratory mucosa determine the outcome of activation versus TH2 immunity in allergic inflammation of the airways
AUTHOR(S): Hall, Gillian; Lund, Lise; Lamb, Jonathan R.; Jarman, Elizabeth R.
CORPORATE SOURCE: Immunobiology Group, MRC Centre for Inflammation Research, Respiratory Medicine Unit, University of Edinburgh Medical School, Edinburgh, UK
SOURCE: Journal of Allergy and Clinical Immunology (2002), 110(6), 883-890
CODEN: JACIBY; ISSN: 0091-6749
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Specific immunotherapy involving systemic injection of allergen, though highly effective, can cause severe side effects due to IgE-mediated activation of effector cells. Allergen-derived **peptides** might provide a safer alternative. We have investigated the use of mucosally delivered **peptide** to induce CD4+ TH2 cell tolerance and thus protect against allergen-induced airway inflammation. The purpose of this study was to investigate whether intranasal administration of an allergen-derived **peptide**, either alone or adsorbed to **chitosan**, can prevent the induction of TH2-mediated pulmonary inflammation after sensitization and challenge of the airways with allergen. Mice were given (intranasally) a **peptide** contg. an immunodominant epitope of the Dermatophagoides pteronyssinus (Der p) 1 allergen, either as **sol.** antigen or adsorbed to **chitosan**, before sensitization and allergen challenge. Pulmonary inflammation, antigen-specific CD4+ T-cell responses, and antibody levels in sera were then detd. Mice given **peptide** adsorbed to **chitosan** had significant redns. in airway eosinophilia, which correlated with reduced levels of IL-4 and IL-5 in the bronchoalveolar lavage fluid. There was decreased recruitment of activated CD4+ T cells into the airways after allergen challenge, which correlated with a loss of Der p 1-specific T-cell cytokine responses in the periphery and the localized prodn. of IL-10 by antigen-specific T cells in bronchial lymph nodes. Induction of peripheral T-cell tolerance was preceded by transient T-cell activation and IFN-.gamma. prodn. Our data demonstrate that suppression of airway inflammation by intranasal administration of **peptide** antigen adsorbed to **chitosan** is initiated by transient T-cell activation and maintained by the prodn. of IL-10 by antigen-specific T cells in the draining lymph nodes.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:667430 CAPLUS
DOCUMENT NUMBER: 137:195570
TITLE: Methods of treating chronic inflammatory diseases using carbonyl trapping agents
INVENTOR(S): Shapiro, Howard K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 473,786, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444221	B1	20020903	US 1999-416120	19991012

PRIORITY APPLN. INFO.: US 1992-906909 B2 19920630
US 1995-473786 B2 19950607
OTHER SOURCE(S): MARPAT 137:195570

AB These and other objects of this invention are achieved by providing a novel method and compns. for the clin. treatment of chronic inflammatory diseases. This invention involves use of systemically administered compns. which include primary amine derivs. of benzoic acid as carbonyl trapping agents. These primary therapeutic agents act by chem. binding to and sequestering the aldehyde and/or ketone products of lipid peroxidn. Increased levels of lipid peroxidn. have been repeatedly demonstrated as a part of the non-enzymic "inflammatory cascade" process which underlies the secondary etiol. of chronic inflammatory diseases. P-Aminobenzoic acid

(or PABA) is an example of the primary therapeutic agent of the present invention. PABA has a small mol. wt., is water **sol.**, has a primary amine group that reacts with carbonyl-contg. metabolites under physiol. conditions and is tolerated by the body in relatively high dosages and for extended periods. The carbonyl sequestering agents are used in combination with at least one co-agent to produce an addnl. beneficial physiol. effect of an anti-inflammatory nature. Such compns. are administered systemically entirely via the oral route. Co-agents of the present invention include anti-oxidants and free radical trapping compds. (e.g., .alpha.-tocopherol), compds. having indirect anti-oxidant activity (e.g., selenium), vitamins (e.g., pyridoxine HCl), compds. which facilitate kidney drug elimination (e.g., glycine), metabolites at risk of depletion (e.g., pantothenic acid), sulfhydryl contg. chems. (e.g., methionine), compds. which facilitate glutathione activity (e.g., N-acetylcysteine), and non-absorbable polyamine co-agents (e.g., **chitosan**).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:391576 CAPLUS
DOCUMENT NUMBER: 136:406913
TITLE: Method for restoring a damaged or degenerated intervertebral disk
INVENTOR(S): Desrosiers, Eric Andre; Chenite, Abdellatif; Berrada, Mohammed; Chaput, Cyril
PATENT ASSIGNEE(S): Bio Syntech Canada Inc., Can.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040070	A2	20020523	WO 2001-CA1623	20011115
WO 2002040070	A3	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002021370	A5	20020527	AU 2002-21370	20011115

PRIORITY APPLN. INFO.:

US 2000-248226P	P	20001115
US 2000-248568P	P	20001116
WO 2001-CA1623	W	20011115

AB The present invention relates to a minimally-invasive method for restoring a damaged or degenerated intervertebral disk at an early stage. The method comprises the step of administering an injectable in situ setting formulation in the nucleus pulposus of the damaged or degenerated disk of a patient. The formulation once injected combines with nucleus matters and host cells, and becomes viscous or gels in situ within the annulus fibrosus of the disk for increasing the thickness and vol. of the damaged or degenerated disk. The formulation is retained within the disk for providing restoration of the damaged or degenerated disk. An acidic soln. made of a water/acetic acid was prepd. for all expts. The pH of this acidic soln. was adjusted to 4.0. High mol. wt. **chitosan** powder was added and dissolved in a vol. of the acidic soln. so as to produce **chitosan** solns. having **chitosan** proportions ranging from 0.5 to 2.0%. Glycerophosphate was added to the **chitosan** solns. and induced a pH increase. **Chitosan** and .beta.-glycerophosphate components individually influenced the pH increase within the aq. solns., and consequently influenced the **sol** to gel transition.

L47 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:142480 CAPLUS
DOCUMENT NUMBER: 136:189357
TITLE: Oral delivery of **peptide**
INVENTOR(S): Kim, Hack-Joo; An, Heung-Man; Cha, Min-Jong
PATENT ASSIGNEE(S): Hyundai Pharmaceutical Ind. Co., Ltd, S. Korea
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013782	A1	20020221	WO 2000-KR892	20000811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000064796	A5	20020225	AU 2000-64796	20000811

PRIORITY APPLN. INFO.: WO 2000-KR892 A 20000811

AB Proliposomes of a peptidyl drug and enteric prepns. contg. said proliposome are disclosed, wherein said proliposome is prepd. by dissolving the peptidyl drug and phospolipid in an org. solvent and coating the resulting soln. with water-**sol**. **chitosan**. The oral delivery system of **peptide** using the proliposome and the enteric prepn. remarkably increases stability and bioavailability of a peptidyl drug. Proliposomes contg. salmon calcitonin were prepd.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:123584 CAPLUS
DOCUMENT NUMBER: 136:184114
TITLE: Preparation of therapeutic water-**soluble** salts of 2-difluoromethyl-2,5-diaminopentanoic acid and polycations
INVENTOR(S): Hebert, Rolland F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002019338	A1	20020214	US 2001-919692	20010731

PRIORITY APPLN. INFO.: US 2000-222420P P 20000801

AB Water-**sol**. salts of 2-difluoromethyl-2,5-diaminopentanoic acid (DFMO) with polycations (e.g., 80% deacetylated **chitosan**) are prepd. and their therapeutic uses described.

L47 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:885702 CAPLUS
DOCUMENT NUMBER: 136:10946
TITLE: Topical agent for dermatological use
INVENTOR(S): Kuriki, Takashi; Nakae, Takashi; Nishimura, Takahisa; Nakayama, Hiroki
PATENT ASSIGNEE(S): Pentapharm Ltd., Switz.; Ezaki Glico Co., Ltd.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091715	A2	20011206	WO 2001-EP6281	20010601
WO 2001091715	A3	20020704		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001342110	A2	20011211	JP 2000-165590	20000602
EP 1289489	A2	20030312	EP 2001-945236	20010601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: JP 2000-165590 A 20000602
WO 2001-EP6281 W 20010601
OTHER SOURCE(S): MARPAT 136:10946
AB The objective of the present invention was to enhance the skin whitening effects and blackening prevention effects and supply safe and stable topical agents for dermatol. use. 4-Hydroxyphenyl-.alpha.-D-glucopyranoside was combined with auxiliary agents such as ascorbic acid and its derivs., crude drugs and its exts., hydroxycarboxylic acid and its salts, oil **sol**. glycyrrhiza ext., gentian ext., phenol derivs. and their salts, placenta ext., kojic acid and its derivs., glucosamine and its derivs., azelaic acid and its derivs., retinol and its derivs., pyridoxine and its derivs., tocopherol and its derivs., **chitosan** and its decompn. products, caffeic acid derivs., hydroxycinnamate and its derivs., Umbelliferae plant exts., mycelial cultures and their exts., plant leaves and their exts. Thus, a toilet oil contained tocopherol 0.2, 4-hydroxycinnamate 0.2, allantoin 0.5, ascorbyl palmitate 0.2, 4-Hydroxyphenyl-.alpha.-D-glucopyranoside 1.0, retinol acetate 0.3, Evening primrose oil 2.0, oil-**sol**. glycyrrhiza ext. 1.0, squalene qs to 100%.

L47 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:380435 CAPLUS
DOCUMENT NUMBER: 135:10066
TITLE: Temperature-controlled and pH-dependent self-gelling biopolymeric aqueous solution
INVENTOR(S): Chenite, Abdellatif; Chaput, Cyril; Wang, Dong; Selmani, Amine
PATENT ASSIGNEE(S): Bio Syntech Canada, Inc., Can.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036000	A1	20010525	WO 2000-CA1341	20001110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1229940	A1	20020814	EP 2000-975711	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-165641P P 19991115
WO 2000-CA1341 W 20001110
AB The present invention relates to a biopolymeric liq. aq. compn. for producing self-gelling systems and gels, which comprises: an acidic water-based medium, 0.1-10 % of a pH-gelling acid-**sol**. biopolymer; and 0.1-10 % of a water-**sol**. mol. having a basic character and a pKa between 6.0 and 8.4, or a water-**sol**. residue or sequence of the mol. having a basic character and a pKa between 6.0 and 8.4. The liq. compn. has a final pH ranging from 5.8 and 7.4, and forms a stable solid and homogeneous gel within a temp. range from 10 to 70.degree.C. The present invention also relates to a method for prepg. the compn. and uses in cosmetics, pharmacol., medicine and/or surgery. **Chitosan** dissolved in 0.1 M HCl soln. was mixed with an aq. soln. of disodium .beta.-glycerophosphate at .apprx. 4.degree.. The obtained clear mixt. was incubated at 37.degree. for 2 h to achieve bulk gelation.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:351168 CAPLUS
DOCUMENT NUMBER: 132:349681
TITLE: High-water-content water-in-oil emulsions containing surfactants and cationic polymers for cosmetic and pharmaceutical applications
INVENTOR(S): Bleckmann, Andreas; Kropke, Rainer; Schneider, Gunther
PATENT ASSIGNEE(S): Beiersdorf Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1002569	A2	20000524	EP 1999-120946	19991102
EP 1002569	A3	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19855153	A1	20000525	DE 1998-19855153	19981130
US 2002146438	A1	20021010	US 1999-436171	19991109
JP 2000154114	A2	20000606	JP 1999-322397	19991112

PRIORITY APPLN. INFO.: DE 1998-19853281 A 19981119
DE 1998-19855153 A 19981130

AB High-water-content water-in-oil emulsions, esp. for cosmetic and medicinal applications, contg. >80 wt.% water and water-**sol**. components and <20 wt.% lipids, emulsifiers, and lipophilic components, consist of at least one surface-active substance of general formula A-O-[CHR1-X-CHR2-O]a-A', in which A and A' are C10-30-alkyl, acyl, and hydroxyacyl, as well as ester functions combined with hydroxyacyl groups, of general formula, -O-C(:O)-R4-CHR3-O[C(:O)R4-CHR3-O]b-C(:O)R4-CHR3OH, R3 is C1-20-alkyl; R4 is branched or linear C1-20-alkylene; b = 0-200; a = 1-100 (most preferably 5-40); X is a single bond or -CH(OR5)-; R1 and R2 = H or Me; R5 = H, C1-20-alkyl or acyl; and further contg. at least one cationic polymer. The cationic polymers are selected from a no. of derivatized biopolymers (e.g., cationic starches, guar gum, **chitosan**, chitin, quaternized polypeptides, and collagen polypeptides) and synthetic polymers (e.g., polymers of diallylammonium salts and quaternized polymers).

L47 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:335033 CAPLUS
DOCUMENT NUMBER: 132:352525
TITLE: Preparations of water-in-oil type emulsions with high water content, containing one or more alkylmethicone copolyols and/or alkyldimethicone copolyols as well as cationic polymers
INVENTOR(S): Bleckmann, Andreas; Kroepke, Rainer; Schneider, Guenther
PATENT ASSIGNEE(S): Beiersdorf Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1000612	A1	20000517	EP 1999-120947	19991102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19852212	A1	20000518	DE 1998-19852212	19981112
US 2001012860	A1	20010809	US 1999-428421	19991028
JP 2000143438	A2	20000523	JP 1999-315414	19991105

PRIORITY APPLN. INFO.: DE 1998-19852212 A 19981112
OTHER SOURCE(S): MARPAT 132:352525

AB Stable water-in-oil emulsions for cosmetic and dermatol. use, contg. .gtoreq.80 wt.% H2O and water-**sol**. substances as inner phase, alkylmethicone copolyols and alkyldimethicone copolyols as surfactants, and a lipid phase (where the surfactant:lipid ratio is 0.10-0.25), can be prepd. with a wide range of viscosities, i.e. as lotions or creams. These emulsions are esp. useful as vehicles for incorporation of antioxidants into the skin. Thus, a water-in-oil cream contained cetyldimethicone copolyol 1.50, caprylic/capric triglyceride 4.00, dicaprylyl ether 3.00, octyldodecanol 3.00, glycerin 3.00, NaCl 0.70, **chitosan** 0.25, 90% lactic acid 0.20, perfume, preservatives, dyes, and H2O to 100.00 wt.%.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:229684 CAPLUS
DOCUMENT NUMBER: 133:109812
TITLE: Enhancement of paracellular drug transport across mucosal epithelial by N-trimethylchitosan chloride
AUTHOR(S): Hamman, J. H.; Stander, M.; Junginger, H. E.; Kotze, A. F.
CORPORATE SOURCE: Department of Pharmaceutics, Potchefstroom University

for Christian Higher Education, Potchefstroom, 2520, S. Afr.
SOURCE: S.T.P. Pharma Sciences (2000), 10(1), 35-38
CODEN: STSSE5; ISSN: 1157-1489
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N-trimethylchitosan chloride (I) is a partially quaternized **chitosan** deriv. with greatly enhanced water **soly**. esp. at neutral and basic pH values. I displayed potential as an absorption enhancer in previous expts. and, like **chitosan**, is able to open the tight junctions of epithelial cells to allow the paracellular transport of large, hydrophilic compds. The **charge** d. of I, as detd. by the degree of quaternization, is an important factor that influences the absorption enhancement properties of this polymer. The effects of **chitosan** and I, with varying degrees of quaternization (12-59%), on the transepithelial elec. resistance of Caco-2 monolayers and the in vitro and in vivo transport of the **peptide** drug, insulin, and the hydrophilic marker [14C]-mannitol are discussed. At a pH of 6.2, all the polymers (I, **chitosan**-HCl, **chitosan** glutamate) are able to markedly reduce the transepithelial elec. resistance of Caco-2 cells. On the contrary, at a pH of 7.4, only I polymers with higher degrees of quaternization (>22%) are able to decrease the transepithelial elec. resistance values significantly. In concordance with the transepithelial elec. resistance results, I polymers with higher degrees of quaternization (>22%) were most effective as enhancers of the in vivo absorption of [14C]-mannitol administered intranasally at a pH of 7.4 to rats. I acts as a novel absorption enhancer, even at basic and neutral pH values where **chitosan** is ineffective as an absorption enhancer, and the degree of I quaternization is an important factor for detg. the absorption-enhancing properties of this polymer, esp. in neutral and basic environments. I may contribute to the development of safe and effective **drug delivery** systems for the non-parenteral administration of large hydrophilic drugs such as **peptides** and proteins.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:176860 CAPLUS
DOCUMENT NUMBER: 133:22272
TITLE: Facile synthesis of a **chitosan** hybrid of a laminin-related **peptide** and its antimetastatic effect in mice
AUTHOR(S): Hojo, Keiko; Maeda, Mitsuko; Mu, Yu; Kamada, Haruhiko; Tsutsumi, Yasuo; Nishiyama, Yasuhiro; Yoshikawa, Tomoko; Kurita, Keisuke; Block, Lawrence H.; Mayumi, Tadanori; Kawasaki, Koichi
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, 651-2180, Japan
SOURCE: Journal of Pharmacy and Pharmacology (2000), 52(1), 67-73
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Laminin, a cell adhesion protein, consists of three **peptide** chains (.alpha.-1, .beta.-1 and .gamma.-1). The .beta.-1 chain contains a Tyr-Ile-Gly-Ser-Arg (YIGSR) sequence that has been found to inhibit exptl. metastasis in mice. We have prepd. a hybrid of a water-**sol**. **chitosan** and a laminin-related **peptide**, and have examd. its inhibitory effect on exptl. metastasis in mice. A laminin-related **peptide**, acetyl-Tyr-Ile-Gly-Ser-Arg-.beta.Ala-OH (Ac-YIGSR.beta.A-OH), was prepd. by a solid-phase method. Ac-YIGSR.beta.A-OH was then reacted with a water-**sol**. **chitosan**. .beta.Ala is a spacer and was placed to avoid racemization of the Arg residue when the **peptide** was coupled with **chitosan**. Although **chitosan** has amino groups, they did not react with the **peptide**. Four methods were tried to achieve a coupling reaction, the diphenylphosphoryl azide method, the diisopropylcarbodiimide/1-hydroxybenzotriazole method, the water-**sol**. carbodiimide (WSC), and the 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) method, but all four methods were unsuccessful. Therefore, a small spacer, tert-butyloxycarbonyl-Gly, was intercalated in **chitosan**, by the TBTU method, to facilitate its coupling with the **peptide**. After removal of the protecting group, the Gly-**chitosan** was coupled with Ac-YIGSR.beta.A-OH by the water-**sol**. carbodiimide method to give Ac-YIGSR.beta.AG-**chitosan**. Conjugation of the **peptide** with the larger

chitosan mol. did not reduce the inhibitory effect of the peptide on exptl. metastasis in mice, it actually potentiated the antimetastatic effect, demonstrating that chitosan may be effective as a drug carrier for peptides.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:139979 ' CAPLUS
DOCUMENT NUMBER: 133:8982
TITLE: Chitosans as nasal absorption enhancers of peptides: comparison between free amine chitosans and soluble salts
AUTHOR(S): Tengamnuay, P.; Sahamethapat, A.; Sailasuta, A.; Mitra, A. K.
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Department of Pharmacy, Chulalongkorn University, Bangkok, Thailand
SOURCE: International Journal of Pharmaceutics (2000), 197(1-2), 53-67
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A total of three free amine chitosans (CS J, CS L and CS H) and two sol. chitosan salts (CS G and CS HCl) were evaluated for their efficacy and safety as nasal absorption enhancers of peptides based on in situ nasal perfusion and subacute histol. evaluation in rat. At 0.5% wt./vol., all chitosans were effective in enhancing the nasal absorption of [d-Arg2]-Kyotorphin, an enzymically stable opioid dipeptide. The enhancing effect of the free amine chitosans increased as the pH was decreased from 6.0 to 4.0 (P<0.05). However, the pH effect was not significant for the two chitosan salts (P0.05), suggesting that their adjuvant activity may be less pH-dependent than the free amine form. CS J and CS G were subsequently selected for further studies. At only 0.02% w/v, their enhancing effect was already significant and comparable to that of 5% w/v hydroxypropyl-.beta.-cyclodextrin (HP-.beta.-CD). Both chitosans at 0.1% caused minimal release of total protein and phosphorus from the rat nasal mucosa, with the values similar to that of 5% HP-.beta.-CD. At 0.5% the two chitosans also stimulated smaller release of lactate dehydrogenase, an intracellular enzyme used as marker of nasal membrane damage, than 1.25% dimethyl-.beta.-cyclodextrin. Morphol. evaluation of the rat nasal mucosa following 2-wk daily administration indicated that the two chitosans (1.0%) produced only mild to moderate irritation. In conclusion, both the free amine and the acid salt forms of chitosans are effective in enhancing the nasal absorption of [d-Arg2]-Kyotorphin and have potential for further studies as a safe and effective nasal absorption enhancer of peptide drugs.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:722417 CAPLUS
DOCUMENT NUMBER: 132:284118
TITLE: Preparation of PEG-grafted chitosan nano-particle for peptide drug carrier
AUTHOR(S): Ohya, Y.; Cai, R.; Nishizawa, H.; Hara, K.; Ouchi, T.
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, 564-8680, Japan
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 655-656
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Entrapment and sustained release of water-sol. insulin into/from PEG-grafted chitosan aggregates are reported.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:674952 CAPLUS
DOCUMENT NUMBER: 132:15553
TITLE: Preparation and drug retention of biodegradable chitosan gel beads
AUTHOR(S): Kofuji, Kyoko; Shibata, Kaori; Murata, Yoshifumi; Miyamoto, Etsuko; Kawashima, Susumu
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Hokuriku

University, Kanazawa, 920-1181, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(10), 1494-1496
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Chitosan** (CS) gel beads contg. drug were prepd. in **amino acid** solns. of pH about 9, despite the requirement for a pH above 12 for gelation in water. This phenomenon was obsd. not only in **amino acid** solns. but also in solns. of compds. having amino groups. A solute concn. of more than 10% was required for prepn. of gel beads at pH 9. Gelation of the CS beads required about 25 to 40 min, depending on the species of **amino acid**. Lidocaine-HCl (LC) as a model drug was retained in the beads to about 20 to 35% of the theor. total amt., despite being a water-**sol**. drug. The release of LC from the CS gel beads was prolonged. The release pattern was not affected by the species of **amino acid** or CS, or the prepn. time.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:626029 CAPLUS
DOCUMENT NUMBER: 131:248264
TITLE: Method for the production of microcapsules
INVENTOR(S): Bayer, Uwe
PATENT ASSIGNEE(S): Aventis Research & Technologies G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948480	A2	19990930	WO 1999-EP1626	19990312
WO 9948480	A3	19991125		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19813011	A1	19991014	DE 1998-19813011	19980325
CA 2325420	AA	19990930	CA 1999-2325420	19990312
AU 9933306	A1	19991018	AU 1999-33306	19990312
AU 733233	B2	20010510		
EP 1066031	A2	20010110	EP 1999-914516	19990312
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 2002507473	T2	20020312	JP 2000-537530	19990312

PRIORITY APPLN. INFO.: DE 1998-19813011 A 19980325
WO 1999-EP1626 W 19990312

AB Microcapsules are produced by atomizing an aq. soln. contg. 0.1-5 wt.% of .gtoreq.1 water-**sol**. polyanion to form liq. droplets. The liq. droplets thus obtained impinge upon a flowing liq. film of a 2nd aq. soln. contg. 0.1-5 wt.% Ca2+ and 0.001-0.4 wt.% **chitosan** (mol. wt. >40,000), and/or 0.1-5 wt.% **chitosan** (av. mol. wt. 500-40,000). The droplets do not agglomerate on exposure to the 2nd soln. The outer layer of these microcapsules is stably crosslinked owing to the use of both Ca2+ and polyanion as crosslinkers. Such microcapsules contg. drugs can be prepd. in a size useful for parenteral sustained-release prepns. Thus, a soln. of Na alginate 9 and FITC-labeled bovine serum albumin in 3 mL aq. 0.9% NaCl soln. was atomized with an ultrasonic atomizer to form 30-.mu.m droplets, and sprayed into an inclined flowing film of a soln. contg. **chitosan** 600 and CaCl2 900 mg in 30 mL H2O. The microcapsules, with a mean size of 90 .mu.m, were washed with 0.9% NaCl soln.; they released 44% of their fluorescent indicator content in 30 days.

L47 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:626028 CAPLUS
DOCUMENT NUMBER: 131:248263
TITLE: Slow release microcapsules
INVENTOR(S): Bayer, Uwe; Hahn, Bernd; Majeres, Anna
PATENT ASSIGNEE(S): Aventis Research & Technologies G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948479	A1	19990930	WO 1999-EP1625	19990312
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19813010	A1	19991014	DE 1998-19813010	19980325
CA 2325554	AA	19990930	CA 1999-2325554	19990312
AU 9928365	A1	19991018	AU 1999-28365	19990312
AU 736941	B2	20010809		
EP 1063970	A1	20010103	EP 1999-908958	19990312
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 2002507472	T2	20020312	JP 2000-537529	19990312

PRIORITY APPLN. INFO.: DE 1998-19813010 A 19980325
WO 1999-EP1625 W 19990312

AB Liq. drops of an aq. soln. contg. .gtoreq.1 water-sol. polyanion are added to a 2nd aq. soln. contg. 0.1-5 wt.% Ca2+ and 0.1-5 wt.% hydrolyzed **chitosan** (no. av. mol. wt. 2200-40,000). Once the addn. of the 1st soln. is complete, the resulting microcapsules remain in the 2nd soln. for 15-360 min, preferably 60-180 min. The hydrolyzed **chitosan** is obtained by partial hydrolysis of a **chitosan** with no. av. mol. wt. >50,000 in an aq. soln. contg. 0.1-4N HCl at 50-95.degree. for 0.5-8 h; the wt. ratio of the HCl soln. to com. **chitosan** is 1-50, and the product of normality of the HCl soln. and the duration of hydrolysis in hours is 0.1-7. The process is carried out in a single step. Thus, 60 g **chitosan** was hydrolyzed with 1500 mL 1.0M HCl at 90.degree. for 4 h and filtered; the filtrate was stored at 2-8.degree. overnight, filtered, and the residue was dissolved in water and freeze dried. A soln. of Na alginate 9 and FITC-labeled bovine serum albumin 6 mg in 3 mL 0.9% NaCl soln., and the mixt. was added dropwise to a soln. of hydrolyzed **chitosan** 300 and CaCl2 450 mg in 15 mL water to produce microcapsules 90 .mu.m in size which released 20% of their fluorescent indicator content in 11 days.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:538104 CAPLUS
DOCUMENT NUMBER: 131:161476
TITLE: Polysaccharide-containing cosmetic or dermatological preparations for protecting sensitive skin from irritation
INVENTOR(S): Nielsen, Jens; Untiedt, Sven; Sauermann, Gerhard; Lanzendoerfer, Ghita; Kielholz, Juergen; Ennen, Joachim; Doerschner, Albrecht; Gohla, Sven; Kaden, Waltraud
PATENT ASSIGNEE(S): Beiersdorf A.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19805827	A1	19990819	DE 1998-19805827	19980213
EP 937454	A2	19990825	EP 1999-102341	19990206
EP 937454	A3	20000315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DE 1998-19805827 19980213

AB Skin irritation and stinging in persons with sensitive skin, resulting from certain skin diseases or from application of deodorants or prepns. contg. .alpha.-hydroxy acids, .alpha.-keto acids, or **amino** **acids** to the skin, are prevented by application of compns. contg. water-**sol**. or water-swellable polysaccharides such as hyaluronic acid or **chitosan**. A suitable compn. contained caprylic/capric triglyceride 11.60, glycerin 3.00, hydrogenated coco glycerides 3.00, fatty alcs. 4.40, glyceryl stearate citrate 4.00, Carbomer 0.40, fucose-rich polysaccharide FG 1000 5.00, arginine-HCl 1.00, preservative, and water to 100.00 wt.%.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:347666 CAPLUS

DOCUMENT NUMBER: 131:102530
TITLE: Preparation of a **chitosan** hybrid of an antimetastatic laminin-related **peptide**
AUTHOR(S): Hojo, Keiko; Maeda, Mitsuko; Mu, Yu; Kamada, Haruhiko; Tsutsumi, Yasuo; Nishiyama, Yasuhiro; Yoshikawa, Tomoko; Kurita, Keisuke; Block, Lawrence H.; Mayumi, Tadanori; Kawasaki, Koichi
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, 651-2180, Japan
SOURCE: Pharmacy and Pharmacology Communications (1999), 5(4), 277-280
CODEN: PPCOFN; ISSN: 1460-8081
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A hybrid of **chitosan** and an anti-metastatic laminin-related **peptide** was prepd. Acetyl-Tyr-Ile-Gly-Ser-Arg-.beta.Ala-OH (Ac-YIGSR.beta.A-OH) was prepd. by a solid-phase method and reacted with a water-**sol**. **chitosan**. **Chitosan** amino groups did not react with the **peptide** using diphenyl-phosphoryl azide, diisopropyl-carbodiimide/1-hydroxy-benzotriazole, water-**sol**. carbodiimide/1-hydroxy-benzotriazole, phosphazo, or 2-(1 H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) methods. A small spacer was therefore put between the **peptide** and the **chitosan**. Tert-Butyloxycarbonyl-Gly (spacer) was reacted with **chitosan** by the TBTU method. After removal of the protecting group, the Gly-**chitosan** was coupled with Ac-YIGSR.beta.A-OH by the water-**sol**. carbodiimide method to give Ac-YIGSR.beta.AG-**chitosan**. The inhibitory effect of the **peptide**-**chitosan** hybrid on exptl. metastasis in mice was not reduced, but actually potentiated, suggesting that **chitosan** may be used as a drug carrier for **peptides**.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:451196 CAPLUS
DOCUMENT NUMBER: 129:183939
TITLE: Design of macromolecular prodrug of 5-fluorouracil using N-acetylpolygalactosamine as a targeting carrier to hepatoma
AUTHOR(S): Ouchi, Tatsuro; Tada, Masahiro; Matsumoto, Mitsuo; Ohya, Yuichi; Hasegawa, Kaname; Arai, Yuichi; Kadowaki, Kiyoshi; Akao, Santaro; Matsumoto, Tatsuji; Suzuki, Shigeo; Suzuki, Masuko
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, and High Technology Research Center, Kansai University, Suita, 564-8680, Japan
SOURCE: Reactive & Functional Polymers (1998), 37(1-3), 235-244
CODEN: RFPOF6; ISSN: 1381-5148
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .alpha.A-1,4-Polygalactosamine (PGA) purified from the culture fluid of Paecilomyces sp. I-1I strain and N-acetylated .alpha.-1,4-polygalactosamine (NAPGA) are **chitosan**- and chitin-like biodegradable, compatible .alpha.-1,4-linked polysaccharides, resp. Partially N-acetylated PGA was found to show the stronger binding activity onto MH134Y hepatoma cells than three kinds of normal lymphocytes, bone marrow, T and B cells from the results of binding assay of 14C-50% N-acetylated PGA in vitro. Since PGA and NAPGA have the unreducing end groups of galactosamine and N-acetyl galactosamine, resp., they were suggested to exhibit the receptor-mediated affinities to hepatoma cells. In order to provide the lysosomotropic macromol. prodrug of fluorouracil (5FU) having a targeting ability to hepatoma, we synthesized water-**sol**. 6-O-carboxymethyl-NAPGA-immobilized 5FUs through Gly-Phe-Leu-Gly, monomethylene spacer groups. The obtained conjugate showed the cathepsin-B-susceptible release behavior of 5FU and then exhibited the stronger cytotoxic activity than free 5FU against HLE hepatoma cells in vitro.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:653286 CAPLUS
DOCUMENT NUMBER: 127:336534
TITLE: N-Trimethyl **chitosan** chloride as a potential absorption enhancer across mucosal surfaces: in vitro evaluation in intestinal epithelial cells (Caco-2)

AUTHOR(S): Kotze, Awie F.; Luessen, Henrik L.; De Leeuw, Bas J.; De Boer, Bert G.; Verhoef, J. Coos; Junginger, Hans E.
CORPORATE SOURCE: Department of Pharmaceutics, Potchefstroom University for Christian Higher Education, Potchefstroom, 2520, S. Afr.
SOURCE: Pharmaceutical Research (1997), 14(9), 1197-1202
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have established that **chitosan** hydrochloride and glutamate are potent absorption enhancers for large hydrophilic compds. across mucosal surfaces. However, these compds. lack **soly**. at neutral pH values. A partially quaternized and well-**sol**. deriv. of **chitosan**, N-trimethylchitosan chloride (I), was synthesized and the effects of this polymer on the transepithelial elec. resistance and permeability of intestinal epithelial cells were investigated in vitro. I was synthesized by reductive methylation and characterized with NMR. The effect of this polymer (1.0-2.5% w/v) on the transepithelial elec. resistance of intestinal epithelial cells, using Caco-2 cell monolayers, was investigated. Permeation of the hydrophilic model compds. [14C]-mannitol (MW 182.2), FITC-Dextran (MW 4400) and the **peptide** drug buserelin (MW 1299.5), in the presence of I (1.5-2.5% w/v), was followed for 3 h. The transport process of the fluorescent marker, FITC-Dextran 4400, across the cell monolayers was visualized with confocal laser scanning microscopy. Viability of the cells was checked with the trypan blue exclusion technique. I is a perfectly water-**sol**., partially quaternized (about 12%) deriv. of **chitosan**. This polymer (1.5-2.5% w/v) caused a pronounced and immediate redn. (25-85%) in the transepithelial elec. resistance of Caco-2 cells. Large increases in the transport rate of [14C]-mannitol (32-60 fold), FITC-Dextran 4400 (167-373 fold) and buserelin (28-73 fold) were demonstrated. Confocal laser scanning microscopy confirmed that I opens the tight junctions of intestinal epithelial cells to allow increased transport of hydrophilic compds. through the paracellular transport pathway. No deleterious effects to the cells could be demonstrated with trypan blue. The potential use of I as an absorption enhancer across mucosal surfaces could be an important contribution towards the development of effective delivery systems for hydrophilic drugs.

L47 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:325992 CAPLUS
DOCUMENT NUMBER: 125:41667
TITLE: **Chitosan** capsules for colon-specific **drug delivery**: improvement of insulin absorption from the rat colon
AUTHOR(S): Tozaki, Hideyuki; Yamamoto, Akira; Fujita, Takuya; Muranishi, Shozo; Terabe, Akira; Muranishi, Shozo; Terabe, Akira; Matsumoto, Takayuki; Suzuki, Tsutomu
CORPORATE SOURCE: Dep. Biopharmaceutics, Kyoto Pharmaceutical Univ., Kyoto, 607, Japan
SOURCE: Drug Delivery System (1996), 11(2), 119-124
CODEN: DDSYEI; ISSN: 0913-5006
PUBLISHER: Nippon DDS Gakkai Jimukyoku
DOCUMENT TYPE: Journal
LANGUAGE: English/Japanese

AB Recently, there has been increasing interest in the targeting of **peptide** and protein drugs to the colon because of the low activity of proteolytic enzymes in the colon. Therefore, many dosage forms such as time controlled-release dosage forms and pH sensitive coating dosage forms were examd. for the specific **drug delivery** to the colon. However, these approaches have recently been shown to lack site specificity, since the variability of pH and small intestinal transit time of these dosage forms were obsd. On the other hand, **chitosan**, which is one of the polysaccharides abundant in nature, is known to be specifically degraded by microorganisms present in the colon. In this study, therefore, **chitosan** capsules contg. insulin were prepd. and the effectiveness of these capsules to colon-specific delivery of insulin was examd. The mean diam. and wt. of these capsules were 35 .times. 1.5 mm and 1.2-1.5 mg, resp. The surface of these capsules was coated with hydroxypropyl methylcellulose phthalate as enteric coating material. The release studies of drug from the **chitosan** were carried out using Japan Pharmacopoeia (J.P.) rotating basket method. 5(6)-Carboxyfluorescein (CF), which was encapsulated in the **chitosan** capsules was used as a water **sol**. model compd. No release of CF from the capsules was obsd. in an artificial gastric juice (pH = 1) and an artificial intestinal juice (pH = 7). However, the release of CF was markedly increased in the presence of rat cecal contents. These findings suggested that the **chitosan** capsules were degraded by the microorganisms in rat cecal contents. The

effectiveness of the **chitosan** capsules of the colon specific delivery of insulin was investigated by an in vivo absorption expt. A marked decrease in plasma glucose levels was obsd. following oral administration of these capsules contg. 20 IU insulin and Na-glycocholate, as compared with the capsules contg. lactose or insulin only. In addn., the **chitosan** capsules contg. insulin and Na-glycocholate were more effective for reducing the plasma glucose levels than the gelatin capsules contg. the same components. Thus, this capsule may be useful carrier for colon-specific delivery of **peptide** including insulin.